

10/728,090

L2 ANSWER 1 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:729555 CAPLUS  
DN 143:199864  
TI Vaginal compositions for treating infections  
IN Ahmad, Nawaz; Patel, Kalpana J.; Wiita, Brinda  
PA Mcneil-Ppc, Inc., USA  
SO PCT Int. Appl., 20 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	WO 2005072774	A1	20050811	WO 2005-US976	20050113
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI US 2004-537154P P 20040116

AB This invention relates to methods, compns. and treatment regimens for applying cooling active ingredients to the perineum of a woman to treat the symptoms of a vaginal or vulvar infection or vulvar pain in order to speed the woman's relief from pain and/or itch. Thus, a gel contained 70% EtOH 5.00, propylene glycol 5.00, sorbitol solution 5.00, hydroxyethyl cellulose 1.50, and water 83.50%.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2005:696643 CAPLUS  
 DN 143:186789  
 TI Nitrosated and/or nitrosylated compounds, compositions and methods of use  
 IN Ellis, James L.  
 PA Nitromed, Inc., USA  
 SO PCT Int. Appl., 84 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005070006	A2	20050804	WO 2005-US2257	20050124
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI US 2004-537918P P 20040122

AB The invention describes novel nitrosated and/or nitrosylated compds. of the invention and pharmaceutically acceptable salts thereof, and novel compns. comprising at least one nitrosated and/or nitrosylated compound of the invention, and, optionally, at least one nitric oxide donor and/or at least one therapeutic agent. The invention also provides novel compns. comprising at least one compound of the invention, and at least one nitric oxide donor and/or at least one therapeutic agent. The invention also provides novel kits comprising at least one compound of the invention, that is optionally nitrosated and/or nitrosylated, and, optionally, at least one nitric oxide donor and/or at least one therapeutic agent. The invention also provides methods for (a) treating bacterial infections; (b) treating viral infections; (c) treating fungal infections; and (d) treating lesions. The nitrosated and/or nitrosylated compds. of the invention are preferably nitrosated and/or nitrosylated antimicrobial compds., nitrosated and/or nitrosylated adenosine antagonists, nitrosated and/or nitrosylated LTB4 antagonists, nitrosated and/or nitrosylated mucoregulators and nitrosated and/or nitrosylated purine agonists. The methods of the invention are preferably for the treatment of bacterial infections associated with pulmonary diseases such as cystic fibrosis.

10/728,090

L2 ANSWER 3 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:572595 CAPLUS  
DN 143:71740  
TI Regimen for the administration of rifamycin-class antibiotics  
IN Michaelis, Arthur F.; Cabana, Bernard E.  
PA USA  
SO U.S. Pat. Appl. Publ., 16 pp.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 2005143409	A1	20050630	US 2004-948608	20040923
	WO 2005030109	A3	20050714	WO 2004-US31317	20040924
	WO 2005030109	C2	20050825		
	W:	AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA			
	RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2003-505855P P 20030924

AB The invention features an ascending dose regimen for the administration of rifamycin-class antibiotics. The dosing regimen can be used to treat bacterial infections and diseases related to infection.

L2 ANSWER 4 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:553224 CAPLUS

DN 143:222187

TI Rifaximin in patients with lactose intolerance

AU Cappello, G.; Marzio, L.

CS Department of Medicine and Ageing, G. d'Annunzio University,  
Chieti-Pescara, Italy

SO Digestive and Liver Disease (2005), 37(5), 316-319

CODEN: DLDIFK; ISSN: 1590-8658

PB Elsevier B.V.

DT Journal

LA English

AB Background. Abdominal symptoms linked to lactose malabsorption may be caused by metabolic activity of colonic bacteria. Rifaximin, a non-absorbable rifampycin derivative, is active against colonic bacteria, it may be useful in the treatment of lactose intolerance. Aim. The aim of this study has been to evaluate short-term rifaximin therapy in patients with lactose intolerance. Methods. Thirty-two patients with lactose intolerance diagnosed using the hydrogen lactose breath test were studied. Fourteen patients received rifaximin 800 mg/day for 10 days, 13 patients followed a diet without milk for 40 days and 5 patients received a placebo for 10 days. Total breath H<sub>2</sub> excretion expressed as area under the curve, and the symptom score were evaluated in all patients at the start, and subsequently after 10 and 40 days. Results. In the 14 patients who received rifaximin for 10 days, area under the curve at day 10 and day 40 was statistically significantly lower than the one computed at basal ( $P < 0.01$ ). Diet reduced area under the curve progressively reaching statistical significance at day 40, while the placebo did not change area under the curve throughout the study. The total symptom score significantly improved after rifaximin and diet. Conclusion. In patients with lactose intolerance, a 10-day therapy with rifaximin as well as 40-day diet without lactose reduces the area under the curve and the symptom score.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:514493 CAPLUS

DN 143:90649

TI A randomized, double-blind, placebo-controlled trial of rifaximin to prevent travelers' diarrhea

AU DuPont, Herbert L.; Jiang, Zhi-Dong; Okhuysen, Pablo C.; Ericsson, Charles D.; de la Cabada, Francisco Javier; Ke, Shi; DuPont, Margaret W.; Martinez-Sandoval, Francisco

CS University of Texas-Houston, Baylor College of Medicine, St. Luke's Episcopal Hospital, and M.D. Anderson Cancer Center, Houston, TX, USA

SO Annals of Internal Medicine (2005), 142(10), 805-812

CODEN: AIMEAS; ISSN: 0003-4819

PB American College of Physicians

DT Journal

LA English

AB Background: Travelers' diarrhea causes substantial morbidity and postinfectious irritable bowel syndrome. Objective: To evaluate nonabsorbable rifaximin for prevention of travelers' diarrhea. Design: Randomized, double-blind, placebo-controlled clin. trial. Setting: Guadalajara, Mexico. Participants: U.S. students. Intervention: On arrival in Guadalajara, Mexico, 210 U.S. adults received rifaximin (200 mg/d, 200 mg twice daily, or 200 mg 3 times daily) or placebo for 2 wk. Measurements: Participants were followed daily for 3 wk for enteric disease and symptoms and daily for 5 wk for drug side effects. Changes in intestinal coliform flora were studied. Results: Travelers' diarrhea developed in 14.74% of participants taking rifaximin and 53.70% of those taking placebo (rate ratio, 0.27 [95% CI, 0.17 to 0.43]). Rifaximin provided 72% and 77% protection against travelers' diarrhea and antibiotic-treated travelers' diarrhea, resp. ( $P < 0.001$  for both), and all rifaximin doses were superior to placebo. In the groups that did not report travelers' diarrhea, rifaximin significantly reduced the occurrence of mild diarrhea ( $P = 0.02$ ) and moderate and severe intestinal problems ( $P = 0.009$  for pain or cramps;  $P = 0.02$  for excessive gas). Rates of adverse events were comparable in the rifaximin and placebo groups. Minimal changes in coliform flora were found during rifaximin therapy. Limitations: Rifaximin safely prevented travelers' diarrhea in Mexico, where most cases are caused by diarrhea-producing *Escherichia coli*. A study is needed in Asia to determine whether rifaximin can prevent diarrhea caused by invasive bacterial pathogens. Conclusions: Rifaximin prevents travelers' diarrhea with minimal changes in fecal flora, and more liberal chemoprophylaxis against this disease should be considered. Future studies should evaluate whether rifaximin is effective in preventing postinfectious irritable bowel syndrome.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 6 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:482583 CAPLUS  
DN 143:13382  
TI Rifaximin ointment  
IN Jia, Wei; Xue, Jing  
PA Heyida Biological Medicine Technology Co., Ltd., Tianjin, Peop. Rep. China  
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given  
CODEN: CNXXEV

DT Patent  
LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	CN 1511526	A	20040714	CN 2002-159131	20021230
PRAI	CN 2002-159131		20021230		

AB The Rifaximin ointment consists of emulsifier matrix, transdermal promoter, humectant and Rifaximin as the active component. The preparation process includes homogeneous mixing of Rifaximin as the active component and emulsifier matrix in the formula amount, the mixing with transdermal promoter and humectant to form orange ointment and final packing. The present invention has wide antibacterial spectrum, miraculous effect in treating conjunctivitis, keratitis, trachoma and other eye diseases and various infectious dermatitis, quick and lasting effect and high curative rate.

10/728,090

L2 ANSWER 7 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:449391 CAPLUS  
DN 143:83450  
TI Rifaximin eye drops  
IN Jia, Wei; Xue, Jing  
PA Heyida Biomedicine Technological Co., Ltd., Tianjin, Peop. Rep. China  
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given  
CODEN: CNXXEV

DT Patent  
LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	CN 1509715	A	20040707	CN 2002-158261	20021225
PRAI	CN 2002-158261		20021225		

AB Eye drops of rifaximin for treating trachoma, conjunctivitis and keratitis are prepared from rifaximin as its active component, solvent (the mixture of alc. and distilled water), the viscosity enhancer chosen from Me cellulose, polyethane diol, poly(vinyl alc.), etc., and sodium phosphate or sodium chloride for regulating pH values and osmotic pressure.

10/728,090

L2 ANSWER 8 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:443593 CAPLUS  
DN 143:83449  
TI Rifaximin sprays  
IN Jia, Wei; Xue, Jing  
PA Heyida Biomedicine Technological Co., Ltd., Tianjin, Peop. Rep. China  
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given  
CODEN: CNXXEV

DT Patent  
LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	CN 1509714	A	20040707	CN 2002-158260	20021225
PRAI	CN 2002-158260		20021225		

AB A rifaximin spray for treating bacterial rhinitis and inflammation of respiratory tract is prepared from rifaximin as active component, and an excipient composed of alc. as solution and propanediol as stabilizer, and the propellant chosen from liquefied gas (fluorochloro paraffin, heptafluoropropane, etc., ) and compressed gas (CO<sub>2</sub>, N, or CO).



L2 ANSWER 9 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:435678 CAPLUS  
DN 143:103454  
TI Separation and Determination of Rifaximin and Quinone-Rifaximin by HPLC  
AU Lu, Hao; Meng, Xiangjun; Wang, Fengqiu; Tang, Hong; Liu, Zhimei  
CS Vocational Technology College, Liaoning College of Traditional Chinese  
Medicine, Shenyang, 110101, Peop. Rep. China  
SO Yaowu Fenxi Zazhi (2004), 24(3), 333-335  
CODEN: YFZADL; ISSN: 0254-1793  
PB Yaowu Fenxi Zazhi Bianji Weiyuanhui  
DT Journal  
LA Chinese  
AB Rifaximin and quinone-rifaximin were separated and analyzed by HPLC using  
Nobelleka Kromasil-C8 chromatog. column (250 mm+4.6 mm, 5  $\mu$ m),  
and using methanol-0.075 mol·L<sup>-1</sup> potassium dihydrogen phosphate-1.0  
mol·L<sup>-1</sup> citron acid solution (60:26:4) as mobile phase at the flow  
rate of 1.0 mL·min<sup>-1</sup>, the detection wavelength of 254 nm and column  
temperature of 15-20 degree C. The result showed that the degree of  
separation of  
rifaximin and quinone-rifaximin was 1.50. This method was suitable for  
the rifaximin anal.

L2 ANSWER 10 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:433378 CAPLUS

DN 143:125929

TI Absorbable vs. non-absorbable antibiotics in the treatment of small intestine bacterial overgrowth in patients with blind-loop syndrome

AU di Stefano, M.; Miceli, E.; Missanelli, A.; Mazzocchi, S.; Corazza, G. R.

CS Department of Medicine, IRCCS'S. Matteo' Hospital, University of Pavia, Pavia, Italy

SO Alimentary Pharmacology and Therapeutics (2005), 21(8), 985-992

CODEN: APTHEN; ISSN: 0269-2813

PB Blackwell Publishing Ltd.

DT Journal

LA English

AB Small intestine bacterial overgrowth is associated with the presence of predisposing conditions, acting through different mechanisms. Therefore, the failure to define a standardized therapy may be due to a methodol. bias: to treat a condition characterized by different pathophysiol. mechanisms with the same pharmacol. approach. Non-absorbable antibiotics could have a lower efficacy than absorbable drugs in patients with blind loops which exclude a portion of the intestine from the transit. The aim was to evaluate the efficacy of absorbable vs. nonabsorbable antibiotics in this subgroup of patients. A group of small intestine bacterial overgrowth patients with total gastrectomy or gastrojejunostomy and blind loop underwent a therapeutic trial comparing rifaximin to metronidazole. Seven patients underwent a course of rifaximin followed by a course of metronidazole on recurrence of symptoms. To compare the effect of the drugs, another two groups of patients underwent two consecutive courses of rifaximin or metronidazole. Hydrogen breath test after glucose administration and symptom severity measurement were performed. Both drugs reduced breath H<sub>2</sub> excretion but a much better improvement was achieved after metronidazole. Symptom improvement was higher after metronidazole. Metronidazole is more effective than rifaximin for the treatment of small intestine bacterial overgrowth associated with the presence of a blind loop.

RE.CNT' 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:430090 CAPLUS

DN 143:108783

TI Travelers' diarrhea: Antimicrobial therapy and chemoprevention

AU DuPont, Herbert L.

CS Internal Medicine at St Luke's Episcopal Hospital, TX, USA

SO Nature Clinical Practice Gastroenterology & Hepatology (2005), 2(4), 191-198

CODEN: NCPGAE; ISSN: 1743-4378

PB Nature Publishing Group

DT Journal; General Review

LA English

AB A review. The use of preventive measures and self-treatment for travelers' diarrhea is routine in regions where the occurrence of diarrhea is predictably high. People traveling to these areas who do not exercise care in their selection of consumed foods and beverages will suffer high rates of illness. Such diarrhea normally affects the traveler for a day, although it can result in chronic postinfectious irritable bowel syndrome. Although systemic antibacterial drugs are effective in preventing diarrhea, their use is not routinely recommended because of side effects and their importance as a therapy for extra-intestinal infections. This review focuses on current and future uses of antibacterial drugs in the prevention and therapy of travelers' diarrhea. Minimally absorbed (<0.4%) rifaximin can effectively reduce the occurrence of travelers' diarrhea without side effects. Bismuth subsalicylate is a useful alternative, although it is less effective than rifaximin for the prevention of travelers' diarrhea and the required doses are less convenient. All people who travel to high-risk areas should take curative antimicrobial agents with them for self-treatment of illness: rifaximin 200 mg three times a day for 3 days, or an absorbable agent such as a fluoroquinolone or azithromycin taken in a single dose initially, with the need for a second or third dose determined by clin. response. Loperamide (up to 8 mg per day for  $\leq 2$  days) can be given with the antibiotic to offer rapid symptomatic improvement. In the future, the ability to evaluate the genetic risk of illness acquisition might allow person-specific recommendations to be made.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:358805 CAPLUS

DN 142:475170

TI Rifaximin, a Peculiar Rifamycin Derivative: Established and Potential Clinical Use Outside the Gastrointestinal Tract

AU Pelosini, Iva; Scarpignato, Carmelo

CS Laboratory of Clinical Pharmacology, Department of Human Anatomy, Pharmacology and Forensic Sciences, School of Medicine and Dentistry, University of Parma, Parma, Italy

SO Chemotherapy (Basel, Switzerland) (2005), 51(Suppl. 1), 122-130  
CODEN: CHTHBK; ISSN: 0009-3157

PB S. Karger AG

DT Journal; General Review

LA English

AB A review. Rifaximin is a poorly absorbed semisynthetic rifamycin derivative with a broad spectrum of antibacterial activity including Gram-pos. and Gram-neg. bacteria, both aerobes and anaerobes. Although originally developed for the treatment of infectious diarrhea, the appreciation of the pathogenic role of gut bacteria in several organic and functional gastrointestinal diseases has increasingly broadened its clin. use. The availability of a topical formulation (a cream containing 5% of the drug) and the lack of transcutaneous absorption pointed out in both animal and human studies has allowed its topical use in skin infections. Furthermore, since the spectrum of antibacterial action of rifaximin includes many organisms (e.g. *Bacteroides bivius*-*disiens*, *Gardnerella vaginalis*, *Haemophilus ducreyi*) causing genital infections, including *Trichomonas vaginalis* and *Chlamydia trachomatis*, its local application in the treatment of bacterial vaginosis (BV) has been attempted. Finally, since periodontal disease, caused by plaque (an aggregate of various bacteria), can be considered a local' infection, intrapocket rifaximin was tried in the treatment of periodontal infections. While the efficacy in pyogenic infections of the skin has been confirmed by several investigations, which showed an improvement of both subjective and objective parameters significantly better than that of the reference drug (i.e. chlortetracycline or oxytetracycline), the usefulness of rifaximin in BV and periodontal disease needs to be further studied in well-designed clin. trials.

RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 13 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:358802 CAPLUS

DN 142:475169

TI Treatment of Small Intestine Bacterial Overgrowth and Related Symptoms by  
Rifaximin

AU Di Stefano, Michele; Corazza, Gino Roberto

CS Gastroenterology Unit, IRCCS 'S. Matteo' Hospital, University of Pavia,  
Pavia, Italy

SO Chemotherapy (Basel, Switzerland) (2005), 51(Suppl. 1), 103-109

CODEN: CHTHBK; ISSN: 0009-3157

PB S. Karger AG

DT Journal; General Review

LA English

AB A review. The treatment of small intestine bacterial overgrowth should  
address different aims: the removal of the predisposing condition,  
guarantee of adequate nutritional support to reintegrate both caloric and  
vitamin requirements and, obviously, suppression of the contaminating  
bacterial flora, which represents the major goal. The polymicrobial nature  
of contaminating flora suggests the administration of wide-spectrum  
antibiotics, but until now there has been no conclusive information on the  
most effective therapeutic approach. In this paper, the efficacy of the  
different therapeutic approaches used is reviewed.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 14 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:358801 CAPLUS

DN 142:475168

TI Management of Inflammatory Bowel Disease: Does Rifaximin Offer Any Promise?

AU Gionchetti, Paolo; Rizzello, Fernando; Morselli, Claudia; Romagnoli, Rossella; Campieri, Massimo

CS IBD Unit, Department of Internal Medicine and Gastroenterology, University of Bologna, Italy

SO Chemotherapy (Basel, Switzerland) (2005), 51(Suppl. 1), 96-102  
CODEN: CHTHBK; ISSN: 0009-3157

PB S. Karger AG

DT Journal; General Review

LA English

AB A review. An increasing number of both clin. and laboratory-derived observations

support the importance of luminal components in driving the inflammatory response in ulcerative colitis and Crohn's disease. Although its role is unclear, antibiotic therapy is commonly used in clin. practice for the treatment of moderately to severely active ulcerative colitis.

Metronidazole and/or ciprofloxacin are currently employed in active Crohn's disease, particularly in patients with colonic involvement and with perianal disease. Rifaximin, a rifamycin-derived antibiotic, is characterized by a wide range of antibacterial activity and a very low systemic absorption. Some preliminary data show its efficacy in severe active ulcerative colitis, pouchitis and prevention of postoperative recurrence in Crohn's disease.

RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 15 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:358800 CAPLUS

DN 142:475167

TI Management of Hepatic Encephalopathy: Role of Rifaximin

AU Zeneroli, Maria Luisa; Avallone, Rossella; Corsi, Lorenzo; Venturini, Ivo; Baraldi, Claudia; Baraldi, Mario

CS Department of Medicine and Medical Specialities, University of Modena and Reggio Emilia, Modena, Italy

SO Chemotherapy (Basel, Switzerland) (2005), 51(Suppl. 1), 90-95

CODEN: CHTHBK; ISSN: 0009-3157

PB S. Karger AG

DT Journal; General Review

LA English

AB A review. Hepatic encephalopathy (HE) is a neuropsychiatric syndrome, which develops in patients with acute or chronic liver failure. It is widely accepted to be due to impairment of hepatic clearance of toxic products from the gut such as ammonia. Accumulation of ammonia induces a glutamate neurotoxicity leading to an increased tone of the  $\gamma$ -aminobutyric acid A (GABA-A) receptor system in the brain which results in HE. Factors either increasing the ammonia levels (protein load, constipation, sepsis, or gastrointestinal bleeding) or potentiating the functional activity of the GABAergic system [natural benzodiazepine-like compds. (NBZDs) or exogenous benzodiazepines] may act as precipitating factors of HE. NBZDs are present in trace amts. in the blood

of

normal subjects and have been increased in the blood of patients with liver cirrhosis, with or without HE. These compds. may derive either from the diet since they have been found in plants, vegetables and animals or from gut bacteria. The observation that intestinal bacterial flora is involved in the production of both primary agent of HE (ammonia) and

precipitating

factors (NBZDs) suggests that the use of nonabsorbable antibiotics such as rifaximin may be useful in preventing episodes of HE in patients with liver cirrhosis.

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 16 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:358798 CAPLUS

DN 142:475166

TI Rifaximin in the Treatment of Infectious Diarrhea

AU Ericsson, Charles D.; DuPont, Herbert L.

CS Department of Internal Medicine and Division of Infectious Diseases,  
University of Texas Houston Medical School, Houston, TX, USA

SO Chemotherapy (Basel, Switzerland) (2005), 51(Suppl. 1), 73-80

CODEN: CHTHBK; ISSN: 0009-3157

PB S. Karger AG

DT Journal; General Review

LA English

AB A review. Rifaximin matches the criteria for an ideal agent for the treatment of infectious diarrhea. It has excellent activity against a broad range of enteropathogens. It is nonabsorbable, which may help explain its excellent side effect profile and lack of emergence of resistance because of high stool levels that are not likely to reach subinhibitory levels before the target Gram-neg. bacilli are killed. It has shown excellent efficacy in numerous clin. trials of bacterial diarrhea. Because of the lack of systemic absorption and minimal adverse reactions, rifaximin should be useful in treating hosts such as pregnant women in whom the currently favored fluoroquinolones are contraindicated. Uses limited to enteric indications and its inherently low propensity to induce sustainable resistance among Gram-neg. flora favor the sustained usefulness of rifaximin in the treatment of enteric infectious syndromes.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT



10/728,090

L2 ANSWER 17 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:358797 CAPLUS  
DN 143:3804  
TI Rifaximin: In vitro and in vivo antibacterial activity. A review  
AU Jiang, Z. D.; DuPont, H. L.  
CS Center for Infectious Diseases, University of Texas-Houston School of  
Public Health, Houston, TX, USA  
SO Chemotherapy (Basel, Switzerland) (2005), 51(Suppl. 1), 67-72  
CODEN: CHTHBK; ISSN: 0009-3157  
PB S. Karger AG  
DT Journal; General Review  
LA English  
AB A review. In vitro inhibitory activity of rifaximin is directed against  
Gram-pos. and Gram-neg., aerobic and anaerobic bacteria. It is effective  
in the treatment of gastrointestinal infections when given orally because  
of the high concentration of the drug remaining in the gut lumen. Laboratory  
investigations have assessed the in vitro activity of rifaximin on  
different bacterial strains isolated from both humans and domestic  
animals. Here, the authors review the in vitro and in vivo activity of  
rifaximin against Gram-neg. rods, Gram-pos. rods and cocci, and their  
resistance to rifaximin. The data suggest that rifaximin is active in  
vitro and in vivo in the treatment of bacterial infections of adults and  
children.  
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 18 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:358796 CAPLUS

DN 142:475165

TI Rifaximin, a Poorly Absorbed Antibiotic: Pharmacology and Clinical Potential

AU Scarpignato, Carmelo; Pelosini, Iva

CS Laboratory of Clinical Pharmacology, Department of Human Anatomy, Pharmacology and Forensic Sciences, School of Medicine and Dentistry, University of Parma, Parma, Italy

SO Chemotherapy (Basel, Switzerland) (2005), 51(Suppl. 1), 36-66  
CODEN: CHTHBK; ISSN: 0009-3157

PB S. Karger AG

DT Journal; General Review

LA English

AB A review. Rifaximin (4-deoxy-4'-methylpyrido[1',2'-1,2]imidazo-[5,4-c]-rifamycin SV) is a synthetic antibiotic designed to modify the parent compound, rifamycin, to achieve low gastrointestinal (GI) absorption while retaining good antibacterial activity. Both exptl. and clin. pharmacol. clearly show that this compound is a nonsystemic antibiotic with a broad spectrum of antibacterial action covering Gram-pos. and Gram-neg. organisms, both aerobes and anaerobes. Being virtually nonabsorbed, its bioavailability within the GI tract is rather high with intraluminal and fecal drug concns. that largely exceed the minimal inhibitory concentration values observed in vitro against a wide range of pathogenic organisms. The GI tract represents, therefore, the primary therapeutic target and GI infections the main indication. The appreciation of the pathogenic role of gut bacteria in several organic and functional GI diseases has increasingly broadened its clin. use, which is now extended to hepatic encephalopathy, small intestine bacterial overgrowth, inflammatory bowel disease and colonic diverticular disease. Potential indications include the irritable bowel syndrome and chronic constipation, Clostridium difficile infection and bowel preparation before colorectal surgery. Because of its antibacterial activity against the microorganism and the lack of strains with primary resistance, some preliminary studies have explored the rifaximin potential for Helicobacter pylori eradication. Oral administration of this drug, by getting rid of enteric bacteria, could also be employed to achieve selective bowel decontamination in acute pancreatitis, liver cirrhosis (thus preventing spontaneous bacterial peritonitis) and nonsteroidal anti-inflammatory drug (NSAID) use (lessening in that way NSAID enteropathy). This antibiotic has, therefore, little value outside the enteric area and this will minimize both antimicrobial resistance and systemic adverse events. Indeed, the drug proved to be safe in all patient populations, including young children. Although rifaximin has stood the test of time, it still attracts the attention of both basic scientists and clinicians. As a matter of fact, with the advancement of the knowledge on microbial-gut interactions in health and disease novel indications and new drug regimens are being explored. Besides widening the clin. use, the research on rifaximin is also focused on the synthesis of new derivs. and on the development of original formulations designed to expand the spectrum of its clin. use.

RE.CNT 278 THERE ARE 278 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

App's

L2 ANSWER 19 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2005:354825 CAPLUS  
 DN 143:199747  
 TI Polymorphous forms of rifaximin, processes for their production and use thereof in medicinal preparations  
 IN Viscomi, Giuseppe C.; Campana, Manuela; Braga, Dario; Confortini, Donatella; Cannata, Vincenzo; Severini, Denis; Righi, Paolo; Rosini, Goggreto  
 PA Alfa Wassermann S, Italy  
 SO N.Z., 27 pp.  
 CODEN: NZXXBT  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	NZ 531622	A	20041029	NZ 2004-531622	20040309
	US 2005101598	A1	20050512	US 2003-728090	20031205
	CA 2460384	AA	20050507	CA 2004-2460384	20040309
	EP 1557421	A1	20050727	EP 2004-5541	20040309
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
	ZA 2004001948	A	20040429	ZA 2004-1948	20040310
	JP 2005139161	A2	20050602	JP 2004-76458	20040317
	BR 2004002382	A	20050628	BR 2004-2382	20040319
	WO 2005044823	A2	20050519	WO 2004-EP12490	20041104
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI IT 2003-MI2144 A 20031107

AB Disclosed herein are  $\alpha$ ,  $\beta$ , and  $\gamma$  polymorphous forms of rifaximin, wherein the formation of the  $\alpha$ ,  $\beta$ , and  $\gamma$  forms depends on the presence of water within the crystallization solvent, on the temperature at which the product is crystallized and the amount of water present into the product at the end of the drying phase. Processes for the production of  $\alpha$ ,  $\beta$ , and  $\gamma$  polymorphs of rifaximin and their pharmaceutical compns. are also disclosed. Thus, raw rifaximin 89.2 g and Et alc. 170 mL were loaded at room temperature into a three-necked flask equipped with mechanic stirrer, thermometer and reflux condenser, then the suspension was heated at  $57 \pm 3^\circ\text{C}$  until complete dissoln. of the solid. The temperature was brought to  $50^\circ\text{C}$  and then demineralized water 51.7 mL were added at this temperature during 30 min. After the end of the addition the temperature was brought to  $30^\circ\text{C}$  in one hour and the suspension was kept for 30 min at this temperature obtaining a plentiful crystallization

The temperature of the suspension was brought to  $40^\circ\text{C}$  and kept at this value during 20 h under stirring and then further lowered to  $0^\circ\text{C}$  during 30 min after which the suspension was immediately filtered. The solid was washed with 240 mL of demineralized water and dried under vacuum at  $65^\circ\text{C}$  until constant weight obtaining rifaximin  $\alpha$  46.7 g with a water content equal to 2.5 %.

10/728,090

L2 ANSWER 20 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:328592 CAPLUS

DN 143:165696

TI Rifaximin: a nonabsorbable rifamycin antibiotic for use in nonsystemic gastrointestinal infections

AU Gerard, Laura; Garey, Kevin W.; DuPont, Herbert L.

CS College of Medicine, University of Houston College of Pharmacy, Houston, TX, 77030, USA

SO Expert Review of Anti-Infective Therapy (2005), 3(2), 201-211

CODEN: ERATCK; ISSN: 1478-7210

PB Future Drugs Ltd.

DT Journal; General Review

LA English

AB A review. Rifaximin is a poorly water-soluble and minimally absorbed (<0.4%) rifamycin with in vitro activity against enteric Gram-neg. bacteria including enteric pathogens. Fecal levels of the drug after 3 days' oral therapy exceed 8000µg/g. Rifaximin is effective in the treatment and prevention of travelers' diarrhea due to Escherichia coli-predominant bacterial pathogens. It shows lower activity against dysenteric forms of bacterial diarrhea. The drug may be useful in other enteric infectious diseases, including Clostridium difficile colitis, pediatric bacterial diarrhea and Helicobacter pylori gastritis and chronic gastrointestinal disorders including hepatic encephalopathy, small bowel bacterial overgrowth, inflammatory-bowel disease, irritable-bowel syndrome and pouchitis. Importantly, rifaximin does not appear to lead to bacterial resistance. Rifaximin has an excellent safety profile and adverse drug reactions have been comparable to those associated with the placebo control agent.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 21 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:318760 CAPLUS

DN 143:146511

TI Pharmacological prophylaxis of hepatic encephalopathy after transjugular intrahepatic portosystemic shunt: a randomized controlled study

AU Riggio, O.; Masini, A.; Efrati, C.; Nicolao, F.; Angeloni, S.; Salvatori, Filippo M.; Bezzi, M.; Attili, Adolfo F.; Merli, M.

CS Department of Clinical Medicine, University of Rome "La Sapienza", Rome, Italy

SO Journal of Hepatology (2005), 42(5), 674-679

CODEN: JOHEEC; ISSN: 0168-8278

PB Elsevier B.V.

DT Journal

LA English

AB Background/Aims: Hepatic encephalopathy is a frequent event after transjugular-intrahepatic-portosystemic-shunt (TIPS), especially during the first months. Aim of this study was to compare two different treatments (lactitol 60 g/day, rifaximin 1200 mg/day) with no-treatment in the prevention of post-TIPS hepatic encephalopathy. Methods: Seventy-five consecutive cirrhotics submitted to TIPS were randomized to receive either one of the above treatments or no-treatment. The main end-point was the occurrence of an episode of overt hepatic encephalopathy during the first month post-TIPS. Before the procedure and weekly thereafter the patients were evaluated by examining their mental status, asterixis, ammonia and trail-making-test Part-A (TMT-A). Results: The three groups were comparable for age, sex, etiol., Child-Pugh-score, post-TIPS porto-systemic gradient, previous hepatic encephalopathy, basal values of ammonia and psychometric performance. Twenty-five patients developed hepatic encephalopathy (33%, CI 95%=22-45%). One-month incidence was similar in the three groups (P=0.97). Previous hepatic encephalopathy (Relative Hazard=3.79;1.27-11.31) and basal-TMT-A Z-score>1.5 (RH=3.55;1.24-10.2) were predictors of post-TIPS encephalopathy at multivariate anal. A <5 mmHg porto-systemic gradient was also significantly related to the occurrence of encephalopathy. Conclusions: Our data show that treatment with lactitol or rifaximin is not effective in the prophylaxis of hepatic encephalopathy during the first month after a TIPS.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 22 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:284340 CAPLUS

DN 142:475259

TI Inductive QSAR descriptors. Distinguishing compounds with antibacterial activity by artificial neural networks

AU Cherkasov, Artem

CS Division of Infectious Diseases, Faculty of Medicine, University of British Columbia, Vancouver, BC, V5Z 3J5, Can.

SO International Journal of Molecular Sciences (2005), 6(1-2), 63-86

CODEN: IJMCFK; ISSN: 1422-0067

URL: <http://www.mdpi.org/ijms/papers/i6010063.pdf>

PB Molecular Diversity Preservation International

DT Journal; (online computer file)

LA English

AB On the basis of the previous models of inductive and steric effects, 'inductive' electronegativity and mol. capacitance, a range of new 'inductive' QSAR descriptors has been derived. These mol. parameters are easily accessible from electronegativities and covalent radii of the constituent atoms and interat. distances and can reflect a variety of aspects of intra- and intermol. interactions. Using 34 'inductive' QSAR descriptors alone we have been able to achieve 93% correct separation of compds. with- and without antibacterial activity (in the set of 657). The elaborated QSAR model based on the Artificial Neural Networks approach has been extensively validated and has confidently assigned antibacterial character to a number of trial antibiotics from the literature.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:256240 CAPLUS

DN 143:71426

TI Efficacy of Mesalazine in the Treatment of Symptomatic Diverticular Disease

AU Di Mario, Francesco; Aragona, Giovanni; Leandro, Gioacchino; Comparato, Giuseppe; Fanigliulo, Libera; Cavallaro, Lucas G.; Cavestro, Giulia M.; Iori, Veronica; Maino, Marta; Moussa, Ali M.; Gnocchi, Alessandro; Mazzocchi, Giancarlo; Franze, Angelo

CS University of Parma, Parma, Italy

SO Digestive Diseases and Sciences (2005), 50(3), 581-586

CODEN: DDSCDJ; ISSN: 0163-2116

PB Springer Science+Business Media, Inc.

DT Journal

LA English

AB We aimed to improve symptoms by means of mesalazine in symptomatic colonic diverticular disease patients. One hundred seventy outpatients (98 M, 72 F; age, 67.1 years; range, 39-84 years) were assigned to four different schedules: rifaximin, 200 mg bid (Group R1: 39 pts), rifaximin, 400 mg bid (Group R2: 43 pts), mesalazine, 400 mg bid (Group M1: 40 pts), and mesalazine, 800 mg bid (Group M2: 48 pts), for 10 days per mo. At baseline and after 3 mo we recorded 11 clin. variables (upper/lower abdominal pain/discomfort, bloating, tenesmus, diarrhea, abdominal tenderness, fever, general illness, nausea, emesis, dysuria), scored from 0 = no symptoms to 3 = severe. The global symptomatic score was the sum of all symptom scores. After 3 mo in all schedules but Group R1, 3 of the 11 symptoms improved ( $P < 0.03$ ); the global score decreased in all groups but Group R1 ( $P < 0.0001$ ). Mesalazine-treated patients had the lowest global score at 3 mo ( $P < 0.001$ ). Mesalazine is as effective as rifaximin (higher dosage schedule) for diminishing some symptoms, but it appears to be better than rifaximin for improving the global score in those patients.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 24 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:244333 CAPLUS

DN 143:307

TI Atom, atom-type, and total nonstochastic and stochastic quadratic fingerprints: a promising approach for modeling of antibacterial activity

AU Marrero-Ponce, Yovani; Medina-Marrero, Ricardo; Torrens, Francisco; Martinez, Yamile; Romero-Zaldivar, Vicente; Castro, Eduardo A.

CS Department of Pharmacy, Faculty of Chemical-Pharmacy, Central University of Las Villas, Santa Clara, 54830, Cuba

SO Bioorganic & Medicinal Chemistry (2005), 13(8), 2881-2899

CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Ltd.

DT Journal

LA English

AB The Topol. Mol. Computer Design (TOMOCOMD-CARDD) approach has been introduced for the classification and design of antimicrobial agents using computer-aided mol. design. For this propose, atom, atom-type, and total quadratic indexes have been generalized to codify chemical structure information. In this sense, stochastic quadratic indexes have been introduced for the description of the mol. structure. These stochastic fingerprints are based on a simple model for the intramol. movement of all valence-bond electrons. In this work, a complete data set containing 1006 antimicrobial agents is collected and presented. Two structure-based antibacterial activity classification models have been generated. The models (including nonstochastic and stochastic indexes) classify correctly more than 90% of 1525 compds. in training sets. These models permit the correct classification of 92.28% and 89.31% of 505 compds. in an external test sets. The approach, also, satisfactorily compares with respect to nine of the most useful models for antimicrobial selection reported to date. Finally, a virtual screening of 87 new compds. reported in the anti-infective field with antibacterial activities is developed showing the ability of the models to identify new leads as antibacterial.

RE.CNT 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



10/728,090

L2 ANSWER 25 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:238834 CAPLUS  
DN 142:291331  
TI Use of tigecycline, alone or in combination with rifampin or other  
antimicrobial agent, to treat osteomyelitis and/or septic arthritis  
IN Testa, Raymond Thomas; Calhoun, Jason; Mader, Jon T.  
PA Wyeth, John, and Brother Ltd., USA; Board of Regents, the University of  
Texas System  
SO PCT Int. Appl., 70 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2005023263	A1	20050317	WO 2004-US28980	20040907
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				
	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				
	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				
	LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				
	NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				
	TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				
	AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				
	EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,				
	SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,				
	SN, TD, TG				

PRAI US 2003-500474P P 20030905

AB The invention discloses a method for treating bone or bone marrow  
infections, joint infection or infection of the tissues surrounding the  
joint by administration of the antibiotic tigecycline alone or in  
combination with a rifamycin antibiotic. In a preferred embodiment, the  
bone or bone marrow infection causes osteomyelitis. In another  
embodiment, the joint infection or infection of the tissues surrounding  
the joint causes septic arthritis. The invention also discloses manufacture of  
a medicament for treatment of bone and/or bone marrow infections, or joint  
infections and/or infections in tissues surrounding the joint with  
tigecycline alone or in combination with rifampin.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 26 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:203802 CAPLUS  
DN 142:360822  
TI Rifaximin soft capsule for inhibiting the RNA synthesis of intestinal  
bacteria  
IN Wu, Jianmei; Chen, Yunfang; Wang, Feng; Zhang, Yang; Wan, Zhongxin  
PA Wanlian Pharmaceutical Co., Ltd., Zhejiang, Peop. Rep. China; Nanjing  
Fantai Institute of Chemicals and Medicine  
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.  
CODEN: CNXXEV  
DT Patent  
LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	CN 1451386	A	20031029	CN 2002-116846	20020412
PRAI	CN 2002-116846		20020412		

AB The oral suspended solution is composed of rifaximin, solvent , surfactant (wetting agent and suspension aid), and medical adjuvant or excipient. The wetting agent is non-ionic surfactant (such as Span, Tween, etc). The suspension aid is beeswax, stearic acid, arabia gum, or synthetic polymer. The oral suspended solution may be used to prepare soft capsule for inhibiting the RNA synthesis of intestinal bacteria.

L2 ANSWER 27 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:162866 CAPLUS  
DN 142:475047  
TI Rifaximin: a new treatment for travelers' diarrhea  
AU Pakyz, Amy L.  
CS Department of Pharmacy, Virginia Commonwealth University, Medical College  
of Virginia, Richmond, VA, 23298-0533, USA  
SO Annals of Pharmacotherapy (2005), 39(2), 284-289  
CODEN: APHRER; ISSN: 1060-0280  
PB Harvey Whitney Books Co.  
DT Journal; General Review  
LA English  
AB A review of the pharmacol., pharmacokinetics, clin. efficacy, adverse  
effects, drug interactions and precautions, and dosing recommendations of  
rifaximin, a new nonabsorbed antimicrobial agent for travelers' diarrhea.  
A MEDLINE search (1966-July 2004) was conducted to extract human and animal  
research data in the English language on rifaximin. Randomized,  
double-blind, placebo-controlled trials were reviewed and included to  
evaluate the efficacy of rifaximin in the treatment of travelers'  
diarrhea. Rifaximin is approved for the treatment of travelers' diarrhea  
in patients  $\geq 12$  years of age with diarrhea caused by noninvasive  
strains of *Escherichia coli*. Rifaximin was superior to placebo and  
trimethoprim/sulfamethoxazole and equivalent to ciprofloxacin in the primary  
clin. endpoint of the time to the last unformed stool passed. Rifaximin  
is a viable alternative to ciprofloxacin for the treatment of travelers'  
diarrhea. As rifaximin is not systemically absorbed, it offers the  
advantage of leading to the development of less resistance compared with  
systemically absorbed antibiotics, in addition to fewer systemic adverse  
effects and drug interactions. However, the potential for  
cross-resistance between rifaximin and rifampin, as well as with other  
classes of antibiotics, is of concern and needs to be elucidated.  
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 28 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:85692 CAPLUS  
DN 142:266750  
TI Dry suspended granule of rifaximin  
IN Jia, Wei; Xue, Jing  
PA Heyida Biological and Medical Science and Technology Co., Ltd., Tianjin,  
Peop. Rep. China  
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 4 pp.  
CODEN: CNXXEV

DT Patent  
LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	CN 1485034	A	20040331	CN 2002-131035	20020926
PRAI	CN 2002-131035		20020926		

AB The dry suspended granule is composed of 1 part rifaximin and 5-35 part medical adjuvant. The medical adjuvant is composed of 1 part suspension aid, 0.05-2 part flocculant, and other adjuvant (such as sucrose, starch, corrective, antiseptic, etc). The suspension aid is microcryst. cellulose, Me cellulose, Na CM-cellulose, hydroxypropyl Me cellulose, Na alginate, arabic gum, and/or pectin. The flocculant is citrate, tartrate, phosphate, and/or  $AlCl_3$ .

10/728,090

L2 ANSWER 29 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:85691 CAPLUS  
DN 142:183429  
TI Rifaximin capsule  
IN Jia, Wei; Xue, Jing  
PA Heyida Biological and Medical Technology Co., Ltd., Tianjin, Peop. Rep. China  
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 4 pp.  
CODEN: CNXXEV

DT Patent  
LA Chinese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	CN 1485033	A	20040331	CN 2002-131034	20020926
PRAI	CN 2002-131034		20020926		

AB The rifaximin capsule is composed of rifaximin and medical adjuvant (at a ratio of 1:0.1-10). The medical adjuvant is lactose, starch, sucrose, saccharin Na, polylactose, polyethylene, polypropylene, polyvinyl alc., polypropylene resin, tri-Et citrate, Mg stearate, carboxymethyl starch, ethanol, SiO<sub>2</sub> gel, talc, kaolin, TiO<sub>2</sub>, and/or SiO<sub>2</sub>.

10/728,090

L2 ANSWER 30 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:1155238 CAPLUS

DN 143:361

TI Influence of rifaximin treatment on the susceptibility of intestinal Gram-negative flora and enterococci

AU DuPont, H. L.; Jiang, Z.-D.

CS Houston School of Public Health, University of Texas, Houston, TX, USA

SO Clinical Microbiology and Infection (2004), 10(11), 1009-1011

CODEN: CMINFM; ISSN: 1198-743X

PB Blackwell Publishing Ltd.

DT Journal

LA English

AB The development of rifaximin- and rifampicin-resistant intestinal coliforms was studied in 27 subjects receiving rifaximin for 3 days by plating stool samples on media containing rifaximin 200 mg/L or rifampicin 64 mg/L before treatment (day 0), after treatment was completed (day 3), and after a further 2 days (day 5). The susceptibility of enterococci grown on day 0 and day 3 was also studied in 71 subjects. Significant increases in antimicrobial-resistant coliform flora were not seen in either the rifaximin-treated or the placebo-treated subjects. Enterococci recovered pre- and post-treatment showed similar susceptibilities. Rifaximin did not select for significant resistance in the Gram-neg. and Gram-pos. intestinal flora during therapy.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 31 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:1142926 CAPLUS

DN 143:19297

TI Clinical effects of rifaximin in patients with hepatic encephalopathy intolerant or nonresponsive to previous lactulose treatment: an open-label, pilot study

AU Sama, Claudia; Morselli-Labate, Antonio Maria; Pianta, Paolo; Lambertini, Laura; Berardi, Sonia; Martini, Gabriella

CS Department of Internal Medicine and Gastroenterology, Alma Mater Studiorum, University of Bologna, Bologna, Italy

SO Current Therapeutic Research (2004), 65(5), 413-422

CODEN: CTCEA9; ISSN: 0011-393X

PB Excerpta Medica, Inc.

DT Journal

LA English

AB Hepatic encephalopathy (HE) is a metabolic-neurophysiol. syndrome that occurs in patients with advanced hepatic disease. One of the main pathogenic mechanisms is represented by circulating toxins produced by the intestinal metabolism of nitrogenous compds. The therapeutic approach to HE is mainly based on drugs that eliminate ammonia-producing bacteria. The aim of this study was to evaluate the effects of the nonabsorbable antibiotic rifaximin in patients with HE who were intolerant or nonresponsive to treatment with an oral, nonabsorbable disaccharide (lactulose). This uncontrolled, open-label, pilot study was conducted at the University of Bologna, Bologna, Italy. Patients aged  $\geq 18$  years with histol. proven liver cirrhosis and HE were studied. All patients were intolerant or nonresponsive to previous treatment with lactulose. Rifaximin tablets were administered to patients at a dosage of 400 mg TID for 10 days. The portal systemic encephalopathy (PSE) index was evaluated at enrollment and at the end of the treatment period. Tolerability was assessed using hematol., biochem., and urinalysis and by recording adverse effects (AEs). Twenty-six patients (18 men, 8 women; mean [SD] age, 55.8 [8.0] years) were enrolled (intolerants,  $n = 17$ ; nonresponders,  $n = 9$ ). All patients completed the study. Significant improvement was shown in most of the 5 components of the PSE index after rifaximin administration in both intolerants and nonresponders. At the end of the 10-day treatment period, the PSE index was significantly reduced in both intolerants and nonresponders. Rifaximin was well tolerated; no clin. relevant AEs were observed during the treatment period. This pilot study of patients with liver cirrhosis and HE who were intolerant or nonresponsive to previous treatment with an oral, nonabsorbable disaccharide suggests that treatment with rifaximin may be considered as an adjuvant or an alternative treatment in reducing HE.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 32 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:722721 CAPLUS  
DN 141:218930  
TI Method of treating diseases associated with abnormal gastrointestinal  
flora  
IN Finegold, Sydney M.  
PA USA  
SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of Ser. No. US 2003-297131,  
filed on 7 Oct 2003 which  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004170617	A1	20040902	US 2003-729949	20031209
	WO 2001093904	A1	20011213	WO 2001-US18071	20010605
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2004062757	A1	20040401	US 2003-297131	20031007
	US 2004167062	A1	20040826	US 2003-741377	20031219
PRAI	US 2000-209712P	P	20000605		
	US 2000-214813P	P	20000628		
	US 2000-240582P	P	20001016		
	WO 2001-US18071	W	20010605		
	US 2003-297131	A2	20031007		
	US 2001-866033	B1	20010525		

AB The invention includes a methods of treating or preventing a disease associated with an abnormal flora. The methods involves treating a patient suffering therefrom with an antimicrobial composition in an amount effective to inhibit or eliminate the bacteria. The antimicrobial composition can be an antibacterial agent and/or a probiotic mixture, and can be administered alone or in combination. Disorders that can be treated by the present methods include Attention Deficit Disorder, Depression, bipolar disorder, Alzheimer's disease, Parkinson's Disease, Whipple's Disease, Tourette's Syndrome, Asperger's syndrome, Pervasive Development Disorder, early onset autism, Rhett's Syndrome, D-lactic acidosis, and schizophrenia. Gastrointestinal disorders can include antimicrobial associated diarrhea or inflammatory bowel diseases such as ulcerative colitis or Crohn's disease.



L2 ANSWER 33 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:673896 CAPLUS

DN 141:254051

TI Corticosteroid-sparing effect of rifaximin, a nonabsorbable oral antibiotic, in active ulcerative colitis: preliminary clinical experience

AU Guslandi, Mario; Giollo, Patrizia; Testoni, Pier Alberto

CS Gastroenterology Unit, S. Raffaele University Hospital, Milan, Italy

SO Current Therapeutic Research (2004), 65(3), 292-296

CODEN: CTCEA9; ISSN: 0011-393X

PB Excerpta Medica, Inc.

DT Journal

LA English

AB The role of enteric flora in the pathogenesis of inflammatory bowel disease constitutes the rationale for the use of antibiotics as adjuvant agents in the treatment of ulcerative colitis (UC) and Crohn's disease. The aim of this study was to assess, in a preliminary fashion, the efficacy of the nonabsorbable antibiotic rifaximin in the treatment of exacerbation of UC in patients with a history of poor corticosteroid tolerance. This open-label pilot study was conducted in the Gastroenterol. Unit, S. Raffaele University Hospital (Milan, Italy). Male and female patients aged 18 to 65 yr with an established diagnosis of left-sided UC who were experiencing a clin. relapse during maintenance treatment with mesalamine and with a history of poor tolerance to corticosteroid therapy were included in the study. They received rifaximin 400 mg BID for 4 wk while continuing to receive mesalamine 2.4 g/d. Disease activity before and after treatment was assessed using Rachmilewitz's Activity Index (RAI). A final RAI score <6 was considered clin. remission. Results: Ten patients (9 men, 1 woman; mean [SD] age, 48.1 [12.3] years [range, 23-64 yr]) participated in the study. The RAI decreased in all patients. Rifaximin treatment induced clin. remission in 7 patients (70%). No adverse effects were reported. Due to our study design, no definitive conclusions can be drawn. However, our preliminary data suggest that rifaximin may be beneficial in the treatment of active UC, obviating corticosteroid therapy in most cases.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 34 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:575012 CAPLUS

DN 141:167528

TI Rifaximin plus mesalazine followed by mesalazine alone is highly effective in obtaining remission of symptomatic uncomplicated diverticular disease

AU Brandimarte, Giovanni; Tursi, Antonio

CS Department of Internal Medicine, Division of Gastroenterology, Cristo Re Hospital, Rome, Italy

SO Medical Science Monitor (2004), 10(5), P170-P173

CODEN: MSMOFR; ISSN: 1234-1010

PB International Scientific Literature, Inc.

DT Journal

LA English

AB Rifaximin plus mesalazine has been showed to be more effective than rifaximin alone in the treatment of recurrent and complicated diverticulitis of the colon. We investigated the effectiveness of the combination rifaximin/mesalazine followed by mesalazine alone to evaluate tolerability and effectiveness in symptomatic remission in uncomplicated diverticular disease. We studied 90 consecutive patients (39 M, 51 F, mean age 67.2 yrs, range 32-91 yrs) with symptomatic uncomplicated diverticular disease. We assessed the following symptoms, scoring them on a quant. scale: (1) constipation, (2) diarrhea, (3) abdominal pain, (4) rectal bleeding, and (5) mucus with stools. All were treated with 800 mg/day rifaximin plus 2.4 gr/day mesalazine for 10 days, followed by 1.6 gr/day mesalazine for 8 wk. They were re-evaluated at the end of mesalazine-alone treatment. Eighty-six patients completed the study (95.56%): the total score decreased from 1439 to 44 ( $p < 0.001$ ). 70 Patients (per-protocol: 81.40% (C.I.: 67-94%); on intention-to-treat: 77.78% (C.I.: 60-85%)) were completely asymptomatic after the 8th week of treatment with mesalazine alone (total symptomatic score: 0), while 16 (per-protocol: 18.60%; on intention-to-treat: 17.77%) showed only slight symptoms (total score: 44). Two (2.22%) showed recurrence of diverticulitis after 4 and 6 wk of treatment with mesalazine alone. Two patients (2.22%) were withdrawn from the study for diarrhea after starting mesalazine. Two others (2.22%) showed transitory pruritus (one) and epigastric pain (one). The results show that rifaximin/mesalazine followed by mesalazine alone is extremely effective in resolving symptoms in patients with symptomatic uncomplicated diverticular disease.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 35 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:550533 CAPLUS

DN 141:82297

TI Immunostimulatory nucleic acids for the treatment of disorders associated with microorganisms, for preventing antibiotic resistance and for treating and preventing warts

IN Bratzler, Robert L.; Petersen, Deanna M.

PA USA

SO U.S. Pat. Appl. Publ., 54 pp., Cont. of U.S. Ser. No. 801,839, abandoned.  
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	US 2004131628	A1	20040708	US 2003-666733	20030919
PRAI	US 2000-187834P	P	20000308		
	US 2001-801839	B1	20010308		

OS MARPAT 141:82297

AB The invention involves administration of an immunostimulatory nucleic acid alone or in combination with an antimicrobial agent for the treatment or prevention of infectious disease associated with microorganisms in subjects, for preventing antibiotic resistance and for treating and preventing warts. The combination of drugs are administered in synergistic amts. or in various dosages or at various time schedules. The invention also relates to kits and compns. concerning the combination of drugs.

10/728,090

L2 ANSWER 36 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:544289 CAPLUS  
DN 141:129008  
TI Determination of rifaximin and its related substances by RP-HPLC  
AU Zhang, Zubing; Li, Zhangwan; Wang, Xian; Li, Changyang  
CS West China School of Pharmacy, Sichuan University, Chengdu, 610041, Peop.  
Rep. China  
SO Huaxi Yaoxue Zazhi (2003), 18(4), 281-283  
CODEN: HYZAE2; ISSN: 1006-0103  
PB Huaxi Yike Daxue Yaoxueyuan  
DT Journal  
LA Chinese  
AB The method for the assay of rifaximin and its related substances was presented. An HP-HPLC method was used with C18 column (5  $\mu$ m, 150 mm x 4.6 mm). The mobile phase was composed of methanol-acetonitrile-0.05M KH<sub>2</sub>PO<sub>4</sub>-0.5M citric acid (50:25:20:5). The detection wavelength was at 254 nm. The linear range of rifaximin was 50-200  $\mu$ g mL<sup>-1</sup> (r = 0.999 9). The average recovery was 99.9%. The method was simple, selective, and reproducible for the assay of rifaximin and its related substances.

L2 ANSWER 37 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:506029 CAPLUS

DN 141:88025

TI Validation of a microbiological method: the STAR protocol, a five-plate test, for the screening of antibiotic residues in milk

AU Gaudin, V.; Maris, P.; Fuselier, R.; Ribouchon, J.-L.; Cadieu, N.; Rault, A.

CS Community Reference Laboratory, AFSSA Fougères, LERMVD, Fougères, F-35302, Fr.

SO Food Additives & Contaminants (2004), 21(5), 422-433

CODEN: FACOEB; ISSN: 0265-203X

PB Taylor & Francis Ltd.

DT Journal

LA English

AB The results of an inhouse laboratory validation of a microbiol. method for the screening of antibiotic residues in milk are presented. The sensitivity of this 5 -plate test, called Screening Test for Antibiotic Residues (STAR), was established by the anal. of milk samples spiked with 66 antibiotics at 8 different concns. Ten different groups of antibiotics were studied: macrolides, aminoglycosides, cephalosporins, penicillins, quinolones, tetracyclines, sulfonamides, lincosamides, phenicolated and miscellaneous drugs. It was shown that 21 antibiotics were detected by the

STAR

protocol at or below the maximum residue limit (MRL), and that a further 27 drugs could be detected at levels from the MRL up to four times the MRL. The sensitivity of the STAR protocol was at or below the MRL for three macrolides, one tetracycline, two aminoglycosides, some sulfonamides, half of the beta-lactams, quinolones, lincosamides, trimethoprim and baquilloprim. Moreover, the STAR protocol was at least twice as sensitive as conventional methods for macrolides, quinolones and tetracyclines. The other antibiotics had limits of detection between four and 150 times the MRL. Each plate was preferentially sensitive for one or two families of antibacterials: the plate *Bacillus cereus* for tetracyclines, the plate *Escherichia coli* for quinolones, the plate *Bacillus subtilis* for aminoglycosides, the plate *Kocuria varians* for macrolides, and the plate *Bacillus stearothermophilus* for sulfonamides and beta-lactams. This method has been used routinely on a day-to-day basis to direct the physicochem. confirmation towards one or two families of antibiotics. Considering the high cost of liquid chromatog. coupled with tandem mass spectrometry detection analyses, the reduction of the range of antibiotics to test for confirmation is a significant gain in time and money.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 38 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:412787 CAPLUS  
DN 140:395549  
TI Controlled and continued delivery of rifaximin and/or other substances  
IN Chiarelli, Piero; Dalseno, Renzo  
PA Italy  
SO PCT Int. Appl., 15 pp.  
CODEN: PIXXD2

DT Patent  
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004041240	A1	20040521	WO 2003-EP12346	20031105
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1560566	A1	20050810	EP 2003-810439	20031105
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	IT 2002-FI212	A	20021105		
	IT 2002-MI2438	A	20021118		
	IT 2003-PI5	A	20030114		
	IT 2003-PI13	A	20030221		
	WO 2003-EP12346	W	20031105		

AB A gum-like device is designed for the controlled and continued delivery of rifaximin, without producing the usually intense red coloration, for the resolution of the infections and the reduction of the inflammation in the oral cavity and in the laryngo-pharyngeal one. The device also protects either the gum or the dental apparatus from acute infections, from the infiltration and the stagnation of the food, and fights chronic infections such as in the periodontal pockets. Moreover, the device can be used to protect the gum from the traumatizing collision that the food exercises during the mastication.

10/728,090

L2 ANSWER 39 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:306984 CAPLUS

DN 141:42696

TI Solution structure of rifaximin and its synthetic derivative rifaximin OR determined by experimental NMR and theoretical simulation methods

AU Martini, Silvia; Bonechi, Claudia; Corbini, Gianfranco; Donati, Alessandro; Rossi, Claudio

CS Department of Chemical and Biosystem Sciences, University of Siena, Siena, 2-53100, Italy

SO Bioorganic & Medicinal Chemistry (2004), 12(9), 2163-2172

CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Ltd.

DT Journal

LA English

AB The solution structure of rifaximin and its derivative rifaximin OR (open ring) was determined by combining NMR exptl. results, theor. simulation of two-dimensional NMR spectra by complete relaxation matrix anal. (corma), and mol. dynamics calcns. In this study the structural rearrangements due to the opening of the aliphatic chain of rifaximin after the reduction process

to form rifaximin OR were investigated. Close spatial proximity of CH3(14) and H28b protons detected by 2D-ROESY spectrum of rifaximin OR, which was not present in rifaximin and the down-field shift of CH3(34) protons in rifaximin OR 1H spectrum were crucial to understand the structural modifications, which occurred within the system. The aliphatic chain of rifaximin OR was found to be no longer sym. with respect to the aromatic moiety. Although no dramatic structural rearrangements were detected, the aliphatic chain moved toward CH3(14), causing a reduction of the aromatic shielding

contribution in particular on CH3(34).

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 40 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:237756 CAPLUS

DN 140:280847

TI Enteroaggregative Escherichia coli diarrhea in travelers: response to rifaximin therapy

AU Infante, Rosa M.; Ericsson, Charles D.; Jiang, Zhi-Dong; Ke, Shi; Steffen, Robert; Riopel, Lise; Sack, David A.; DuPont, Herbert L.

CS Center for Infectious Diseases, The University of Texas - Houston School of Public Health and Medical School, Houston, TX, USA

SO Clinical Gastroenterology and Hepatology (2004), 2(2), 135-138  
CODEN: CGHLAW; ISSN: 1542-3565

PB Elsevier Inc.

DT Journal

LA English

AB Background and Aims: The authors have recently shown that enteroaggregative Escherichia coli (EAEC) strains commonly cause travelers' diarrhea. The study was designed to determine whether U.S. travelers with EAEC diarrhea responded to rifaximin therapy. Methods: In a multicenter placebo-controlled clin. trial of travelers' diarrhea without non-EAEC pathogens the authors evaluated 2 doses of rifaximin. EAEC was sought in stool samples in enrolled subjects by HEp-2 cell assay. Response to rifaximin (both groups combined) and placebo were evaluated in EAEC-pos. and EAEC-neg. patient groups. Results: Compared with placebo, rifaximin shortened the postenrollment illness in travelers with EAEC diarrhea (median, 22 vs. 72 h;  $P = 0.03$ ). In subjects with EAEC-neg. diarrhea, the median duration of posttreatment diarrhea was shorter with rifaximin (33 h) than with placebo (52 h), but this difference was not significantly different ( $P = 0.14$ ). Conclusions: Improvement of EAEC-mediated diarrhea with antibiotic treatment supports the pathogenicity of this organism in travelers to developing countries. The study provides information on the value of the poorly absorbed drug rifaximin in therapy of travelers' diarrhea.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



L2 ANSWER 41 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:151845 CAPLUS

DN 141:254421

TI Endotoxemia and benzodiazepine-like substances in compensated cirrhotic patients: a randomized study comparing the effect of rifaximine alone and in association with a symbiotic preparation

AU Lighthouse, J.; Naito, Y.; Helmy, A.; Hotten, P.; Fuji, H.; Min, C. H.; Yoshioka, M.; Marotta, F.

CS Noguchi Mem. Res. Med. Institute, Nagoya, Japan

SO Hepatology Research (2004), 28(3), 155-160

CODEN: HPRSFM; ISSN: 1386-6346

PB Elsevier

DT Journal

LA English

AB Aim: The aim of the present investigation was to test study benzodiazepines (BZDs) profile in patients with viral cirrhosis under different combinations of rifaximine and of a novel symbiotic. Methods: Our study groups consisted of 30 patients with a confirmed diagnosis of HCV-related Child B liver cirrhosis. Patients were randomly allocated into three groups: rifaximine 400 mg t.i.d. for 2 wk; (B) SCM-III (Lactobacillus acidophilus, Lactobacillus helveticus and Bifidobacteria in a ion- and vitamin-enriched medium, Named srl, Italy) 10 mL t.i.d. for 2 wk; (C) rifaximine 400 mg t.i.d. for 1 wk followed by SCM-III 10 mL t.i.d. for 5 wk. At weekly interval, blood samples were withdrawn to test BZD-like substances, ammonia and endotoxin. Results: Rifaximine treatment brought about a significant early drop of BZDs ( $P < 0.01$  vs. pre-treatment and vs. control) till fourth week of observation when a gradual increase took place with return to pre-treatment values at the sixth week. Symbiotic treatment was comparably effective while given to patients but significantly elevated BZDs level were noted starting from the third week. Similar phenomena were noted for endotoxin and ammonia although symbiotic seemed more effective against endotoxin and rifaximine against ammonia increase. However, the sequential treatment rifaximine-symbiotic brought about a sustained normalization of BZDs, ammonia and endotoxin throughout the 6-wk study. Conclusion: The present pilot study suggests that a rifaximine-symbiotic regimen could be an effective tool in compensated liver cirrhosis to limit some triggering factors of hepatic encephalopathy while being amenable to long-term use and devoid of significant side effects.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 42 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:41226 CAPLUS

DN 140:105321

TI Methods and compositions relating to isoleucine boroproline compounds

IN Adams, Sharlene; Miller, Glenn T.; Jesson, Michael I.; Jones, Barry

PA Point Therapeutics, Inc., USA

SO PCT Int. Appl., 152 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004658	A2	20040115	WO 2003-US21405	20030709
	WO 2004004658	A3	20050804		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZW				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2491466	AA	20040115	CA 2003-2491466	20030709
	US 2004077601	A1	20040422	US 2003-616694	20030709
	US 2005084490	A1	20050421	US 2003-616409	20030709
PRAI	US 2002-394856P	P	20020709		
	US 2002-414978P	P	20021001		
	US 2003-466435P	P	20030428		
	WO 2003-US21405	W	20030709		

OS MARPAT 140:105321

AB A method for treating subjects with, inter alia, abnormal cell proliferation or infectious disease using agents of formula (I,  $\text{AmNHCH}(\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3)\text{COAlR}$ ) (where Am and Al are amino acids and R = organo boronates, organo phosphonates, fluoroalkyl ketones, alphaketos, N-peptidyl-O-(acylhydroxylamines), azapeptides, azetidines, fluoroolefins dipeptide isosteres, peptidyl ( $\alpha$ -aminoalkyl) phosphonate esters, aminoacyl pyrrolidine-2-nitriles and 4-cyanothiazolidides) is claimed. Methods for stimulating an immune response using the compds. of the invention are also claimed. Compns. containing Ile-boroPro compds. are also provided as are kits containing the compns. The invention embraces the use of these compds. alone or in combination with other therapeutic agents.

L2 ANSWER 43 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:9365 CAPLUS  
DN 140:82434  
TI RP-HPLC determination of rifaximin  
AU Wang, Jian; Wang, Jin-ling; Bao, Han  
CS The Second Hospital of Nanjing City Affiliated to Medical College of  
Southeast University, Nanjing, 210003, Peop. Rep. China  
SO Zhongguo Xinyao Zazhi (2003), 12(11), 932-934  
CODEN: ZXZHA6; ISSN: 1003-3734  
PB Zhongguo Xinyao Zazhishe  
DT Journal  
LA Chinese  
AB Objective: To establish a RP-HPLC method for the determination of rifaximin.  
Methods: The ODS column was used mobile phase was the mixture of  
methanol-0.075mol·L<sup>-1</sup> KH<sub>2</sub>PO<sub>4</sub>-1.0mol·L<sup>-1</sup> citric acid solution  
(75:26:4), the detection wavelength was set at 254nm and the flow rate was  
1mL·min<sup>-1</sup>. Results: The linear relation was good at  
10.0-100.0μg·mL<sup>-1</sup> (r = 0.999 9), the content of sample solution for  
test was stable for 8h. The relative standard deviation for reproducibility  
within a day was 0.24% and within 3 day was 0.50%. The recovery was  
99.2%. Conclusion: This method is rapid, simple and accurate.

L2 ANSWER 44 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:701418 CAPLUS

DN 140:122707

TI Spontaneous bacterial peritonitis associated with experimental cirrhosis: comparative effect of different therapeutic options on endotoxemia and hemodynamic derangement

AU Marotta, F.; Naito, Y.; Helmy, A.; Oliva, E.; Minelli, E.; Yoshioka, M.; Min, C. H.

CS Immunology Research Institute & Clinic, Nagoya, Japan

SO Chinese Journal of Digestive Diseases (2003), 4(2), 69-74

CODEN: CJDDA9; ISSN: 1443-9611

PB Blackwell Publishing Asia Pty Ltd.

DT Journal

LA English

AB OBJECTIVE: The aim of this investigation was to assess the role of different therapeutic options aimed at modifying the gut microecol. in exptl. liver cirrhosis in view of the cytokine cascade and splanchnic and systemic hemodynamics. METHODS: Cirrhosis was induced in male Sprague-Dawley rats by carbon tetrachloride (CCl<sub>4</sub>). After the 6th week of CCL<sub>4</sub> administration rats were divided into 5 groups for the remaining 6 wk: (A) saline b.i.d; (B) lactulose 0.5 g b.i.d.; (C) rifaximin 1 mg b.i.d; (D) 2 mL b.i.d of a probiotic mixture and (E) 1 wk of rifaximin followed by 5 wk of probiotic. RESULTS: Rats with cirrhosis and ascites showed a significantly high concentration of either portal, splanchnic and systemic endotoxin, as well as plasma TNF- $\alpha$  concentration ( $P < 0.05$ ). Rifaximin alone, rifaximin plus probiotic or probiotic alone significantly decreased the plasma endotoxin concentration at each of the three tested sites, as well as the plasma concentration of TNF- $\alpha$  ( $P < 0.01$ ). Total Gram-neg. aerobic bacteria count in the stool markedly decreased together with a significant increase of the enterococcal population in the rifaximin plus probiotic group and, to a lesser extent, in the other treatment groups. Treated rats showed a significantly decreased occurrence of bacterial peritonitis and the rifaximin plus probiotic treatment was the most effective regimen. Each of the treatments significantly reduced the percentage of pos. culture of either mesenteric lymph node or portal vein samples, rifaximin plus probiotic being the most effective. As compared with healthy control rats, those with cirrhosis showed a significantly lower mean arterial pressure and systemic vascular resistance, but a higher cardiac index and portal pressure. Spontaneous bacterial peritonitis further worsened the systemic vascular resistance, but this was partly improved by the rifaximin plus probiotic treatment. CONCLUSION: These data suggest that the association of a nonabsorbable antibiotic with a probiotic beneficially affects the abnormal systemic vasodilatory response in the course of severe liver cirrhosis, probably through the effects on endotoxin and indirect inhibition of TNF- $\alpha$  release.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 45 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:675123 CAPLUS

DN 139:255223

TI Rifaximin reduces EEG relative beta power in patients with minimal hepatic encephalopathy: preliminary findings

AU Del Piccolo, F.; Amodio, P.; Mapelli, D.; Montagnese, S.; Pellegrini, A.; Valenti, P.; Ferrieri, A.; Gatta, A.

CS Department of Clinical and Experimental Medicine, Clinical Medicine 5, University of Padova, Italy

SO Encephalopathy and Nitrogen Metabolism in Liver Failure, [International Symposium on Hepatic Encephalopathy and Nitrogen Metabolism], 11th, Amsterdam, Netherlands, May 30-June 1, 2002 (2003), Meeting Date 2002, 361-367. Editor(s): Jones, E. Anthony; Meijer, Alfred J.; Chamuleau, Robert A. F. M. Publisher: Kluwer Academic Publishers, Dordrecht, Neth. CODEN: 69EJU2; ISBN: 1-4020-1157-1

DT Conference

LA English

AB Plasma benzodiazepine-like compds. (Bzd-L-Cs) are detectable in normal subjects, and their concentration increases in patients with progressive chronic

liver disease. Bzd-L-Cs may precipitate hepatic encephalopathy (HE). The intestinal bacterial flora has been implicated in the production of Bzd-L-Cs and treatment with rifaximin may reduce their levels in patients with cirrhosis. Bzd-L-Cs increase EEG beta activity. We determined whether rifaximin treatment reduces EEG beta activity in patients with cirrhosis and minimal HE (mHE). Eleven one-week courses of treatment, 8 rifaximin 600 to 1200 mg/day and 3 placebo, were randomly and blindly assigned to 5 cirrhotic patients with mHE (abnormal number connection test, symbol digit test or EEG). After treatment, the relative beta power of the EEG decreased in the rifaximin-treated group (Wilcoxon paired test:  $Z = 2.1$ ,  $p = 0.03$ ), but not in the placebo-treated group ( $Z = 1.07$ ,  $p$  NS). The EEG mean dominant frequency did not change. Psychometric tests did not change significantly; there was a trend for NCT to improve in the rifaximin-treated group (Wilcoxon paired test:  $Z = 1.7$ ,  $p = 0.08$ ). In conclusion, the reduction of EEG beta activity in rifaximin-treated patients with mHE is compatible with previous observations that demonstrated a decrease in Bzd-L-C blood levels in patients with cirrhosis, who underwent rifaximin treatment.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 46 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:616803 CAPLUS

DN 139:304409

TI Susceptibility to rifaximin of *Vibrio cholerae* strains from different geographical areas

AU Scrascia, Maria; Forcillo, Maria; Maimone, Francesco; Pazzani, Carlo

CS Sezione di Genetica, Dipartimento di Anatomia Patologica e di Genetica, Universita di Bari, 70126, Italy

SO Journal of Antimicrobial Chemotherapy (2003), 52(2), 303-305

CODEN: JACHDX; ISSN: 0305-7453

PB Oxford University Press

DT Journal

LA English

AB Four hundred and eight clin. strains of *Vibrio cholerae* isolated from different geog. areas and with different antimicrobial resistance patterns were tested for susceptibility to rifaximin, a non-absorbable antibiotic active in vitro against Gram-neg. bacteria. The MICs ranged from 0.5 to 4 mg/L for all strains. These values and the pharmacokinetic properties suggest rifaximin as an attractive antimicrobial agent for cholera.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 47 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:515507 CAPLUS

DN 139:190699

TI Effects of probiotics, lactitol and rifaximin on intestinal flora and fecal excretion of organic acids in cirrhotic patients

AU Hotten, P.; Marotta, F.; Naito, Y.; Minelli, E.; Helmy, A.; Lighthouse, J.; Fuji, H.; Fesce, E.

CS Sumitomo Memorial Hospital, Nagoya, Japan

SO Chinese Journal of Digestive Diseases (2003), 4(1), 13-18

CODEN: CJDDA9; ISSN: 1443-9611

PB Blackwell Publishing Asia Pty Ltd.

DT Journal

LA English

AB Aim: The aim of the present study was to assess fecal organic acid excretion and gut flora changes in a group of patients with compensated liver cirrhosis without hepatic encephalopathy by comparing probiotic therapy with more common therapeutic approaches. Methods: Thirty patients with compensated Child B liver cirrhosis were allocated into one of three matched groups, which were randomly given one of three 3-wk oral treatments: (i) lactitol 20 g t.i.d.; (ii) 400 mg rifaximin b.i.d.; or (iii) the synbiotic SCM-III (Microflorana-F, NAMED, Lesmo, Italy) 10 mL t.i.d. Stool samples were collected at both the time of entry into the study and at the end of the trial period for the assessment of intestinal bacterial flora and for the determination of fecal pH and of organic acid concentration

Results: All three tested compds. significantly increased the total anaerobic bacterial count to the same extent. The change was mainly due to a reduction in the Bacteriodes population and an expansion of the bifidobacteria population. However, only SCM-III significantly decreased the total count of Bacteroides and Clostridium. Lactitol and SCM-III decreased (to a similar extent) the fecal pH compared with healthy controls and with pretreatment values ( $P < 0.05$ ). Both lactitol and SCM-III produced a significant increase in the fecal concentration of acetic

acid

and lactic acid. However, only SCM-III decreased the fecal concentration of toxic short-chain fatty acids. Conclusions: In the present clin. study, we confirmed the findings from an in vitro study of enhanced-non-toxic organic acid recovery from stools during treatment with nonabsorbable disaccharides. In the present study, we found that lactitol did not produce any significant effect on Bacteroides and Clostridium, whereas the specific bacterial counts of such species significantly decreased only in the group treated with the synbiotic. These data suggest a potential role of synbiotics in the long term treatment of chronic liver disease.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 48 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:443449 CAPLUS

DN 140:22664

TI Therapy of travelers' diarrhea with rifaximin on various continents

AU Steffen, Robert; Sack, David A.; Riopel, Lise; Jiang, Zhi-Dong; Sturchler, Matus; Ericsson, Charles D.; Lowe, Brett; Waiyaki, Peter; White, Mike; DuPont, Herbert L.

CS Division of Communicable Diseases, Institute of Social and Preventive Medicine of the University, Zurich, CH-8006, Switz.

SO American Journal of Gastroenterology (2003), 98(5), 1073-1078

CODEN: AJGAAR; ISSN: 0002-9270

PB Elsevier Science Inc.

DT Journal

LA English

AB Our aim was to compare the efficacy and safety of rifaximin, a virtually nonabsorbed antibiotic, 600 and 1200 mg per day, with placebo in patients with travelers' diarrhea. This was a multicenter, 1:1:1 randomized, parallel-group, double-blind study, conducted in Antigua, Guatemala; Guadalajara and Morelia, Mexico; and the coast of Kenya north and south of Mombasa. Adult patients with acute travelers' diarrhea were recruited; exclusion criteria included primarily medication that could influence the outcome. Subjects were treated for 3 days, three times daily; follow-up lasted 5 days. For each 24-h period, the subjects completed a diary card. Pre- and posttreatment stool, blood, and urinesamples were assessed. Among the 380 volunteers, median time to the last unformed stool was 32.5 and 32.9 h in both rifaximin groups, compared with 60.0 h with placebo ( $p = 0.0001$ ). Also, secondary clin. outcome measures were favorably influenced by the active agent. No relevant side effects were reported. Rifaximin is efficacious and safe for treatment of travelers' diarrhea at daily doses of 600 mg or higher.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



L2 ANSWER 49 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:212123 CAPLUS

DN 139:285707

TI Inhibition of intestinal bacterial translocation with rifaximin modulates lamina propria monocytic cells reactivity and protects against inflammation in a rodent model of colitis

AU Fiorucci, Stefano; Distrutti, Eleonora; Mencarelli, Andrea; Barbanti, Miriam; Palazzini, Ernesto; Morelli, Antonio

CS Sperimentale e Farmacologia, Dipartimento di Medicina Clinica, Clinica di Gastroenterologia ed Epatologia, Universita di Perugia, Perugia, I-06100, Italy

SO Digestion (2002), 66(4), 246-256

CODEN: DIGEBW; ISSN: 0012-2823

PB S. Karger AG

DT Journal

LA English

AB A modification of the intestinal flora and an increased bacterial translocation is a common finding in patients with inflammatory bowel disease as well as in animal model of colitis. Rifaximin, a non-absorbable derivative of rifamycin, is an effective antibiotic that acts by inhibiting bacterial RNA synthesis. In the present study, we investigated the effect of the administration of rifaximin (10, 30 and 50 mg/kg/day) or prednisolone (10 mg/kg/day) in 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis in mice. Colitis was induced in mice by intrarectal administration of TNBS (1.5 mg/mouse in 50% ethanol) and disease severity assessed clin. and by histol. scoring of colon damage, determination of IL-2, IL-12, interferon (IFN)- $\gamma$  and TNF- $\alpha$  (protein and mRNA) and myeloperoxidase (MPO) activity in the colon. Cytokines production by the lamina propria mononuclear cells (LPMC) and luminal bacteria were also measured. Rifaximin administration (30 or 50 mg/kg/day) increased survival rates of colitic mice and reduced colitis severity as demonstrated by improvement of wasting syndrome, histol. scores, decrease in colon IL-2, IL-12, IFN- $\gamma$  and TNF- $\alpha$  (protein and mRNA) levels, and diminished colon MPO activity. Rifaximin administration caused a significant reduction of colon bacterial translocation towards mesenteric lymph nodes. LPMC obtained from rifaximin-treated mice released significantly lower amount of IFN- $\gamma$  in response to ex vivo stimulation with agonistic anti-CD3 and anti-CD28 antibodies. Rifaximin (50 mg/kg/day) significantly accelerates recovery in mice with established colitis. Luminal bacterial microflora plays a role in the pathogenesis of TNBS-induced colitis in mice. Rifaximin administration reduces the development of colitis and accelerates healing of established disease by preventing bacterial translocation.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 50 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:188645 CAPLUS

DN 139:301330

TI A randomized controlled multicenter clinical trial on treatment of acute infectious enterocolitis with rifaximin

AU Yang, Weihong; Zhou, Liya; Lin, Sanren; Yu, Yanyan; Cheng, Liufang; Yuan, Yaorong

CS Department of Gastroenterology, The Third Hospital, Peking University, Beijing, 100083, Peop. Rep. China

SO Zhongguo Linchuang Yaolixue Zazhi (2002), 18(4), 263-267

CODEN: ZLYZE9; ISSN: 1001-6821

PB Beijing Yike Daxue, Linchuang Yaoli Yanjiuso

DT Journal

LA Chinese

AB The clin. efficacy and safety of rifaximin for treatment of acute infectious enterocolitis were evaluated. A total of 203 patients with acute infectious enterocolitis entered a multi-center, randomized, comparative trial. Patients were divided into two groups: treated with rifaximin as a treated group and ciprofloxacin (200 mg tid in the first day and bid in the following two days) as a control, resp. 101 Patients were enrolled in rifaximin group and 102 patients were enrolled in control group. The results showed that the rate and time of diarrhea disappear, the normalization rate of stool routine, stool character and defecation frequency, and the relieve rate of accompanied symptoms were similar in the two groups. The total efficacy rate was 94.1% and 96.1% in the treatment and controlled group, resp. The incidences of adverse reaction were 4.0% and 3.9% in the two groups, resp. There were no significant differences between the two groups in total efficacy rate and incidence of adverse reaction. Rifaximin was effective and safe agent in the treatment of acute infectious enterocolitis.

10/728,090

L2 ANSWER 51 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:177597 CAPLUS  
DN 139:69073  
TI NMR and MS of Rifaximin  
AU Meng, Xiang-Jun; Li, Na-Ran; Lu, Jie; Tang, Hong  
CS Medicines Laboratory, Shenyang Medical College, Shenyang, 110031, Peop.  
Rep. China  
SO Guangpu Shiyanshi (2003), 20(1), 31-34  
CODEN: GUSHEH; ISSN: 1004-8138  
PB Guangpu Shiyanshi Bianjibu  
DT Journal  
LA Chinese  
AB The structure of Rifaximin was investigated by  $^1\text{H}$ NMR,  $^{13}\text{C}$ NMR, and MS. The detail MS fragmentation process was discussed.

L2 ANSWER 52 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:930960 CAPLUS

DN 139:224133

TI Comparison of rifaximin and lactitol in the treatment of acute hepatic encephalopathy: results of a randomized, double-blind, double-dummy, controlled clinical trial

AU Mas, Antoni; Rodes, Juan; Sunyer, Lourdes; Rodrigo, Luis; Planas, Ramon; Vargas, Victor; Castells, Lluís; Rodriguez-Martinez, Dolores; Fernandez-Rodriguez, Conrado; Coll, Ignasi; Pardo, Albert

CS Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Hospital Clinic, Institut de Malalties Digestives, Liver Unit, University of Barcelona, Barcelona, Spain

SO Journal of Hepatology (2003), 38(1), 51-58  
CODEN: JOHEEC; ISSN: 0168-8278

PB Elsevier Science Ltd.

DT Journal

LA English

AB The efficacy and safety of rifaximin in comparison with lactitol in the treatment of acute hepatic encephalopathy was assessed in a prospective randomized, double-blind, double-dummy, controlled trial. A total of 103 patients with grade I-III acute hepatic encephalopathy were randomized to receive rifaximin (50 patients, 1200 mg/day) or lactitol (53 patients, 60 g/day) for 5-10 days. Changes in the portal-systemic encephalopathy (PSE) index on entry and at the end of the study were used to evaluate the efficacy of the two therapies. Both groups were comparable before treatment with regard to demog. data and characteristics of the hepatic encephalopathy episode. The global efficacy of both therapies was similar: 81.6% in the rifaximin group and 80.4% in the lactitol group showed improvement or total regression of the episode. A significantly better evolution of the PSE index was observed in the rifaximin group, due to a greater effect of rifaximin in two components of the index: EEG abnormalities and ammonia levels. No serious adverse events related to either treatment were found during the study. Rifaximin may be considered a useful and safe alternative therapy to lactitol in the treatment of acute hepatic encephalopathy in cirrhosis.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 53 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:697999 CAPLUS

DN 137:226204

TI Long-term treatment with mesalazine and rifaximin versus rifaximin alone for patients with recurrent attacks of acute diverticulitis of colon

AU Tursi, A.; Brandimarte, G.; Daffina, R.

CS Emergency Division, "L. Bonomo" Hospital, Rome, Italy

SO Digestive and Liver Disease (2002), 34(7), 510-515

CODEN: DLDIFK; ISSN: 1590-8658

PB W. B. Saunders

DT Journal

LA English

AB The aim was to compare efficacy of combined therapy with rifaximin and mesalazine vs. rifaximin alone in treatment of patients with recurrent diverticulitis in order to evaluate rapidity in improvement of symptoms, regulation of bowel attacks, prevention of recurrence of diverticulitis. A total of 218 consecutive eligible patients (131 males, 87 females age 64.3 yr, range 51-79), affected by diverticulitis were monitored. Of these, 109 patients were treated with rifaximin 400 mg bid plus mesalazine 800 mg tid for 7 days, followed by rifaximin 400 mg bid plus mesalazine 800 mg bid for 7 days/mo (group A); 109 patients were treated with rifaximin 400 mg bid for 7 days, followed by rifaximin 400 mg bid for 7 days/mo (group B). Colonoscopy was performed after 3, 6 and 12 mo of therapy. At end of follow-up, 193 patients were fully compliant to therapy. Two patients died during study (1 in group A, 1 in group B), while four patients were lost to follow-up [1 in group A (0.91 %) and 3 in group B (2.75%)]. The only side-effects recorded were transient urticaria (1 in group B, 0.91 %) and epigastric pain (9 in group A, 8.25%). Severity of symptoms improved significantly in group A vs. group B within 3 mo ( $p < 0.005$ ,  $p < 0.001$  and  $p < 0.0001$  and  $p < 0.0005$  at 3, 6, 9 and 12 mo, resp.). Bowel habits improved significantly in group A vs. group B within 3 mo ( $p < 0.005$ ,  $p < 0.0005$ ,  $p < 0.001$  and  $p < 0.0001$  at 3, 6, 9 and 12 mo resp.). Symptomatic recurrence of diverticulitis occurred in 3 patients in group A, while 13 patients showed recurrence of diverticulitis in group B ( $p < 0.005$ ) during follow-up. This study clearly shows that rifaximin plus mesalazine are more effective than rifaximin alone in resolution of symptoms and prevention of recurrence of diverticulitis.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 54 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:697621 CAPLUS

DN 137:369871

TI Spectroscopic investigation of the conformational properties and self-association behavior of natural compounds in solution

AU Martini, Silvia; Magnani, Agnese; Corti, Piero; Corbini, Gianfranco;

Lampariello, Raffaella; Picchi, Maria Pia; Ricci, Maso; Bonechi, Claudia

CS Department of Chemical and Biosystem Sciences, University of Siena, Siena, 53100, Italy

SO Spectroscopy Letters (2002), 35(4), 581-602

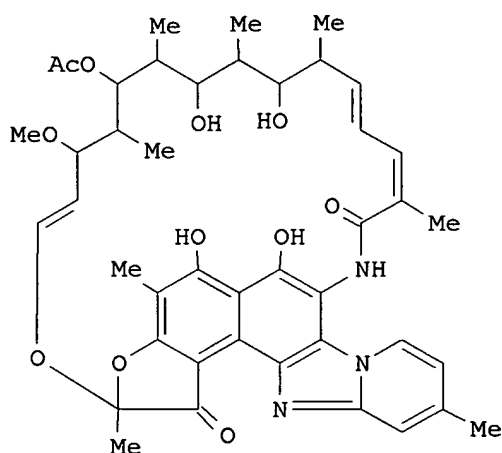
CODEN: SPLEBX; ISSN: 0038-7010

PB Marcel Dekker, Inc.

DT Journal

LA English

GI



I

AB The conformational properties and self-association behavior of rifaximin (I) and rifaximin OR (Open Ring) were investigated in solution by NMR and IR spectroscopy. The dependence of proton chemical shift on concentration and temperature

were analyzed to study the self-association process. IR spectra of rifaximin and rifaximin OR were also used at different concns. to investigate the entity of specific inter- and intramol. interactions. Although similar in structure the two mols. had different chemical properties in solution This could be of some interest in view of the biol. importance of this class of antibiotic mols.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 55 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:576997 CAPLUS

DN 137:134548

TI Effects of rifaximin administration on the intestinal microbiota in patients with ulcerative colitis

AU Brigidi, P.; Swennen, E.; Rizzello, F.; Bozzolasco, M.; Matteuzzi, D.

CS Department of Pharmaceutical Sciences, University of Bologna, Bologna, 40126, Italy

SO Journal of Chemotherapy (Firenze, Italy) (2002), 14(3), 290-295

CODEN: JCHEEU; ISSN: 1120-009X

PB E.I.F.T. srl

DT Journal

LA English

AB The effect of rifaximin on the intestinal bacterial population was studied in a clin. trial. Twelve patients with ulcerative colitis were administered rifaximin 1800 mg/day in 3 treatment periods of 10 days, each followed by 25 days of wash-out. Fecal samples were collected at the beginning and at the end of each treatment period to perform microbiol. exams. Titer variations of enterococci, coliforms, lactobacilli, bifidobacteria, Bacteroides spp., and Clostridium perfringens as well as their susceptibility to rifaximin during the different phases of the study were evaluated. The presence of Candida spp. was also monitored. After each wash-out period, concns. of the intestinal microbial groups tested returned to initial values, showing that the administration of high doses of rifaximin does not significantly modify the colonic microbiota. Rifaximin-resistant isolates were also found, particularly in bacteria belonging to Bifidobacterium genus, included as probiotics in several fermented foods and in pharmaceutical prepsns.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 56 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:426876 CAPLUS

DN 137:149790

TI Structure-Based Classification of Antibacterial Activity

AU Cronin, Mark T. D.; Aptula, Aynur O.; Dearden, John C.; Duffy, Judith C.;  
Netzeva, Tatiana I.; Patel, Hiren; Rowe, Philip H.; Schultz, T. Wayne;  
Worth, Andrew P.; Voutzoulidis, Konstantinos; Schueuermann, Gerit

CS School of Pharmacy and Chemistry, Liverpool John Moores University,  
Liverpool, L3 3AF, UK

SO Journal of Chemical Information and Computer Sciences (2002), 42(4),  
869-878

CODEN: JCISD8; ISSN: 0095-2338

PB American Chemical Society

DT Journal

LA English

AB The aim of this study was to develop a simple quant. structure-activity  
relation (QSAR) for the classification and prediction of antibacterial  
activity, to enable in silico screening. To this end a database of 661  
comps., classified according to whether they had antibacterial activity,  
and for which a total of 167 physicochem. and structural descriptors were  
calculated, was analyzed. To identify descriptors that allowed separation of  
the  
two classes (i.e. those comps. with and without antibacterial activity),  
anal. of variance was utilized and models were developed using linear  
discriminant and binary logistic regression analyses. Model predictivity  
was assessed and validated by the random removal of 30% of the comps. to  
form a test set, for which predictions were made from the model. The  
results of the analyses indicated that six descriptors, accounting for  
hydrophobicity and inter- and intramol. hydrogen bonding, provided  
excellent separation of the data. Logistic regression anal. was shown to model  
the data slightly more accurately than discriminant anal.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT



10/728,090

L2 ANSWER 57 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:249477 CAPLUS

DN 137:75745

TI Antimicrobial susceptibility of *Streptococcus* species isolated from clinical mastitis in dairy cows

AU Guerin-Faublee, Veronique; Tardy, Florence; Bouveron, Clarisse; Carret, Gerard

CS Departement de Sante Publique, Laboratoire de Bacteriologie, Ecole Nationale Veterinaire de Lyon, Marcy l'Etoile, 69280, Fr.

SO International Journal of Antimicrobial Agents (2002), 19(3), 219-226  
CODEN: IAAGEA; ISSN: 0924-8579

PB Elsevier Science B.V.

DT Journal

LA English

AB The antimicrobial susceptibility was determined for 50 *Streptococcus uberis*, 42 *S. dysgalactiae* subsp. *dysgalactiae* and 8 *S. agalactiae* strains isolated from cow mastitis. Only 27% of the strains were susceptible to all antimicrobial compds. tested. Resistance to tetracycline was most frequent (particularly for *S. dysgalactiae* strains), then macrolide and/or lincomycin resistance. High level resistance to streptomycin and kanamycin was detected. All *S. dysgalactiae* and *S. agalactiae* strains were susceptible to  $\beta$ -lactams but 44% of the *S. uberis* strains showed an elevated penicillin G MIC. All strains were susceptible to chloramphenicol and rifampicin.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 58 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2002:107167 CAPLUS  
DN 136:156464  
TI Therapeutic polyesters and polyamides  
IN Uhrich, Kathryn E.  
PA Rutgers, the State University of New Jersey, USA  
SO PCT Int. Appl., 51 pp.  
CODEN: PIXXD2

DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2002009768	A2	20020207	WO 2001-US23747	20010727
	WO 2002009768	A3	20021107		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2417389	AA	20020207	CA 2001-2417389	20010727
	AU 2001078055	A5	20020213	AU 2001-78055	20010727
	US 2002071822	A1	20020613	US 2001-917194	20010727
	US 6689350	B2	20040210		
	EP 1309354	A2	20030514	EP 2001-956013	20010727
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	JP 2004505063	T2	20040219	JP 2002-515320	20010727
	US 2005031577	A1	20050210	US 2004-753048	20040106
PRAI	US 2000-220707P	P	20000727		
	US 2001-261337P	P	20010112		
	US 2001-917194	A3	20010727		
	WO 2001-US23747	W	20010727		

AB Polymers (i.e. polyesters, polyamides, and polythioesters or a mixture thereof) which degrade hydrolytically into biol. active compds. are provided. Methods of producing these polymers, intermediates useful for preparing these polymers, and methods of using these polymers to deliver biol. active compds. to a host are also provided. The biol. active compound is a non-steroidal anti-inflammatory drug, antibacterial, antifungal, anticancer, antithrombotic, immunosuppressant, or analgesic. For example, morphine was copolymd. with a diacid chloride to provide a polyester.

L2 ANSWER 59 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:926053 CAPLUS

DN 136:193730

TI Rifaximin versus ciprofloxacin for the treatment of traveler's diarrhea: A randomized, double-blind clinical trial

AU DuPont, Herbert L.; Jiang, Zhi-Dong; Ericsson, Charles D.; Adachi, Javier A.; Mathewson, John J.; DuPont, Margaret W.; Palazzini, Ernesto; Riopel, Lise M.; Ashley, David; Martinez-Sandoval, Francisco

CS Center for Infectious Diseases, The University of Texas-Houston School of Public Health and Medical School, Houston, USA

SO Clinical Infectious Diseases (2001), 33(11), 1807-1815

CODEN: CIDIEL; ISSN: 1058-4838

PB University of Chicago Press

DT Journal

LA English

AB Rifaximin is a poorly absorbed rifamycin derivative under investigation for treatment of infectious diarrhea. Adult students from the United States in Mexico and international tourists in Jamaica were randomized to receive either rifaximin (400 mg twice per day) or ciprofloxacin (500 mg twice per day) for 3 days, following a double-blinded model, from June 1997 to Sept. 1998. A total of 187 subjects with diarrhea were studied. Time from initiation of therapy to passage of last unformed stool was comparable for those receiving rifaximin or ciprofloxacin (median, 25.7 h vs. 25.0 h, resp.). There was no significant difference in the proportion of subjects in the 2 groups with respect to clin. improvement during the first 24 h ( $P = .199$ ), failure to respond to treatment ( $P = .411$ ), or microbiol. cure ( $P = .222$ ). The incidence of adverse events was low and similar in each group. Rifaximin is a safe and effective alternative to ciprofloxacin in the treatment of traveler's diarrhea.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 60 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:855108 CAPLUS

DN 137:103414

TI Effects of daily oral administration of rifaximin and neomycin on fecal aerobic flora in rats

AU Miglioli, P. A.; Allerberger, F.; Calabro, G. B.; Gaion, R. M.

CS Department of Pharmacology and Anaesthesiology, University of Padua, Padua, Italy

SO Pharmacological Research (2001), 44(5), 373-375

CODEN: PHMREP; ISSN: 1043-6618

PB Academic Press

DT Journal

LA English

AB Rats received 50 mg rifaximin/kg/day or 50 mg neomycin/kg/day, orally, for 3 days. Fecal specimens, collected on day 3, were cultured for the quant. and qual. determination of aerobic microorganisms. Rifaximin markedly reduced the

number of total aerobic bacteria and Salmonellae; neomycin reduced Salmonellae, but did not change total aerobic bacterial count. The binding of neomycin to feces could explain this limited activity, which does not correlate with the in vitro susceptibility of the microorganisms involved. These results confirm that rifaximin is suitable for oral treatment to reduce selected bacteria in the gut. (c) 2001 The Italian Pharmacological Society.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 61 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:454213 CAPLUS  
DN 135:177901  
TI In vitro activity of rifaximin against bacterial enteropathogens causing  
diarrhea in children under 5 years of age in Ifakara, Tanzania  
AU Sierra, Josep M.; Navia, Margarita M.; Vargas, Martha; Urassa, Honorati;  
Schellemborg, David; Gascon, Joaquim; Vila, Jordi; Ruiz, Joaquim  
CS Servicio de Microbiologia, Hospital Clinic, IDIBAPS, Barcelona, 08036,  
Spain  
SO Journal of Antimicrobial Chemotherapy (2001), 47(6), 904-905  
CODEN: JACHDX; ISSN: 0305-7453  
PB Oxford University Press  
DT Journal  
LA English  
AB Rifaximin was shown to be an effective antibiotic against Escherichia and  
Shigella strains responsible for diarrhea in Tanzanian children.  
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 62 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:137173 CAPLUS

DN 134:178396

TI Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

IN Del Soldato, Piero

PA Nicox S.A., Fr.

SO PCT Int. Appl., 94 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001012584	A2	20010222	WO 2000-EP7225	20000727
	WO 2001012584	A3	20020829		
	W:	AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2381409	AA	20010222	CA 2000-2381409	20000727
	BR 2000013264	A	20020416	BR 2000-13264	20000727
	EP 1252133	A2	20021030	EP 2000-953102	20000727
	EP 1252133	B1	20050608		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
	JP 2003515526	T2	20030507	JP 2001-516885	20000727
	NZ 516889	A	20041029	NZ 2000-516889	20000727
	AU 781643	B2	20050602	AU 2000-65670	20000727
	AT 297375	E	20050615	AT 2000-953102	20000727
	ZA 2002000628	A	20030423	ZA 2002-628	20020123
	NO 2002000623	A	20020409	NO 2002-623	20020208
PRAI	IT 1999-MI1817	A	19990812		
	WO 2000-EP7225	W	20000727		

OS MARPAT 134:178396

AB Compds. or their salts of general formula (I): A-B-N(O)<sub>s</sub> wherein: s is an integer equal to 1 or 2; A = R-T<sub>1</sub>-, wherein R is the drug radical and T<sub>1</sub> = (CO)t or (X)t', wherein X = O, S, NR<sub>1c</sub>, R<sub>1c</sub> is H or a linear or branched alkyl or a free valence, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1; B = -TB -X<sub>2</sub>-O- wherein TB = (CO) when t = 0, TB = X when t' = 0, X being as above defined; X<sub>2</sub>, bivalent radical, is such that the precursor drug of A and the precursor of B meet resp. the pharmacol. tests described in the description. Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

L2 ANSWER 63 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:122600 CAPLUS

DN 134:289966

TI Getting discriminant functions of antibacterial activity from physicochemical and topological parameters

AU Mishra, Rama K.; Garcia-Domenech, R.; Galvez, J.

CS Department of Chemistry, Sambalpur University, Jyoti-Vihar, 768 019, India

SO Journal of Chemical Information and Computer Sciences (2001), 41(2), 387-393

CODEN: JCISD8; ISSN: 0095-2338

PB American Chemical Society

DT Journal

LA English

AB Linear discriminant anal. has been demonstrated to be a very useful tool in the selection and design of new drugs. Up to now we have used it through the search of a topol. pattern of activity. In this work our goal is to calculate a complete set of physicochem. parameters using semiempirical (quantum chemical) calcns. as well as topol. indexes (TIs) and try to find out any discriminant function for antibacterial activity through the combined use of both types of descriptors. The physicochem. parameters, such as heat of formation, HOMO, LUMO, dipole moment, polarizability, hyperpolarizability, PM3 generated IR vibrational frequencies, etc., were calculated using PM3 Hamiltonian implemented within the MOPAC97 package. Among the TIs, connectivity as well as topol. charge indexes stands as the most representatives. The obtained results suggest that one of the maxima and min. vibrational frequencies play an important role in the antibacterial activity. These frequencies are associated with the torsional mol. vibration (N3) and the stretching vibration (N5) of X-H groups (X = C, N, O). Furthermore, the differences between the maxima and min. values showed an even better discriminant ability than the values themselves. The addnl. use of the topol. indexes provided a clear improvement in the discriminant function and also provided a straightforward way to predict the values of such frequencies, so that the results can be applied to a large set of compds. searching for new candidates as antibacterials.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 64 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:115322 CAPLUS

DN 134:159863

TI Methods of diagnosing or treating irritable bowel syndrome and other disorders caused by small intestinal bacterial overgrowth

IN Lin, Henry C.; Pimental, Mark

PA Cedars-Sinai Medical Center, USA

SO PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001011077	A2	20010215	WO 2000-US22030	20000811
	WO 2001011077	A3	20010830		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6861053	B1	20050301	US 1999-374142	19990811
	EP 1200828	A2	20020502	EP 2000-952739	20000811
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	US 2003031625	A1	20030213	US 2002-107240	20020326
	US 6805852	B2	20041019		
	US 2005014693	A1	20050120	US 2004-853824	20040526
	US 2005008652	A1	20050113	US 2004-915193	20040810
PRAI	US 1999-374142	A	19990811		
	US 1995-442843	B1	19950517		
	US 1997-832307	A1	19970403		
	US 1999-359583	B2	19990722		
	US 1999-374143	A2	19990811		
	US 1999-420046	B2	19991018		
	US 2000-546119	A2	20000410		
	WO 2000-US22030	W	20000811		
	WO 2000-US22168	A	20000811		
	WO 2001-US11238	A	20010407		
	US 2001-837797	A3	20010417		
	US 2002-107240	A3	20020326		
	US 2004-810020	A1	20040326		

AB Disclosed is a method of diagnosing irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, attention deficit/hyperactivity disorder, autoimmune diseases, such as multiple sclerosis and systemic lupus erythematosus, or Crohn's disease, which involves detecting the presence of small intestinal bacterial overgrowth (SIBO) in a human subject having at least one symptom associated with a suspected diagnosis of any of those diagnostic categories. Also disclosed is a method of treating these disorders, and other disorders caused by SIBO, that involves at least partially eradicating a SIBO condition in the human subject. The method includes administration of anti-microbial or probiotic agents, or normalizing intestinal motility by employing a prokinetic agent. The method improves symptoms, including hyperalgesia related to SIBO and disorders caused by SIBO. Also disclosed is a kit for the diagnosis or treatment of irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, attention deficit/hyperactivity



10/728,090

disorder, autoimmune diseases, or Crohn's disease. Breath hydrogen testing was done on patients after an overnight fast and swallowing Chronulac formula containing 10 g lactulose. Breath samples were analyzed for hydrogen content with a gas chromatograph.

10/728,090

L2 ANSWER 65 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:64596 CAPLUS  
DN 134:234222  
TI In vitro activity of rifaximin against enteropathogens producing  
traveler's diarrhea  
AU Sierra, Josep M.; Ruiz, Joaquin; Navia, Margarita M.; Vargas, Martha;  
Gascon, Joaquim; Vila, Jordi  
CS Institut Clinic d'Infeccions i Immunologia IDIBAPS Hospital Clinic School  
of Medicine University of Barcelona, Barcelona, 08036, Spain  
SO Antimicrobial Agents and Chemotherapy (2001), 45(2), 643-644  
CODEN: AMACCQ; ISSN: 0066-4804  
PB American Society for Microbiology  
DT Journal  
LA English  
AB Definitely good in vitro activity of rifaximin was observed against several  
enteropathogens which cause traveler's diarrhea, e.g. Escherichia coli,  
Shigella spp., and Salmonella spp. The MIC50 and MIC90 values of  
rifaximin ranged from 4 to 8 and from 4 to 16 µg/mL for all tested  
bacteria with the exception of Yersinia enterocolitica and Campylobacter  
jejuni. These values were very similar to those for rifampin.  
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 66 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:15518 CAPLUS

DN 134:175413

TI In vitro antimicrobial susceptibility testing of bacterial enteropathogens causing traveler's diarrhea in four geographic regions

AU Gomi, Harumi; Jiang, Zhi-Dong; Adachi, Javier A.; Ashley, David; Lowe, Brett; Verenkar, Mangala P.; Steffen, Robert; Dupont, Herbert L.

CS Center for Infectious Diseases, University of Texas-Houston Medical School and School of Public Health, Houston, TX, USA

SO Antimicrobial Agents and Chemotherapy (2001), 45(1), 212-216

CODEN: AMACCQ; ISSN: 0066-4804

PB American Society for Microbiology

DT Journal

LA English

AB The emergence of resistant enteropathogens has been reported worldwide. Few data are available on the contemporary in vitro activities of commonly used antimicrobial agents against enteropathogens causing traveler's diarrhea (TD). The susceptibility patterns of antimicrobial agents currently available or under evaluation against pathogens causing TD in four different areas of the world were evaluated. Pathogens were identified in stool samples from U.S., Canadian, or European adults (18 yr of age or older) with TD during 1997, visiting India, Mexico, Jamaica, or Kenya. MICs of 11 different antimicrobials were determined against 284 bacterial enteropathogens by the agar dilution method. Ciprofloxacin, levofloxacin, ceftriaxone, and azithromycin were highly active in vitro against the enteropathogens, while traditional antimicrobials such as ampicillin, trimethoprim, and trimethoprim/sulfamethoxazole showed high levels and high frequencies of resistance. Rifaximin, a promising and poorly absorbable drug, had an MIC at which 90% of the strains tested were inhibited of 32 µg/mL, 250 times lower than the concentration of this drug in the stools. Amdinocillin, nalidixic acid, and doxycycline showed moderate activity. Fluoroquinolones are still the drugs of choice for TD in most regions of the world, although our study has a limitation due to the lack of Escherichia coli samples from Kenya and possible bias in selection of the patients for evaluation. Azithromycin and rifaximin should be considered as promising new agents. The widespread in vitro resistance of the traditional antimicrobial agents reported since the 1980s and the new finding of resistance to fluoroquinolones in Southeast Asia are the main reasons for monitoring carefully the antimicrobial susceptibility patterns worldwide and for developing and evaluating new antimicrobial agents for the treatment of TD.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 67 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:742057 CAPLUS

DN 133:309791

TI Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

IN Del Soldato, Piero

PA Nicox S.A., Fr.

SO PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000061541	A2	20001019	WO 2000-EP3239	20000411
	WO 2000061541	A3	20010927		
	W:	AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	IT 1311923	B1	20020320	IT 1999-MI752	19990413
	CA 2370425	AA	20001019	CA 2000-2370425	20000411
	BR 2000009703	A	20020108	BR 2000-9703	20000411
	EP 1169298	A2	20020109	EP 2000-926870	20000411
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	JP 2002541236	T2	20021203	JP 2000-610818	20000411
	TR 200102928	T2	20021223	TR 2001-200102928	20000411
	NZ 514270	A	20040227	NZ 2000-514270	20000411
	RU 2237057	C2	20040927	RU 2001-127574	20000411
	AU 777579	B2	20041021	AU 2000-45474	20000411
	ZA 2001008126	A	20030403	ZA 2001-8126	20011003
	NO 2001004928	A	20011213	NO 2001-4928	20011010
PRAI	IT 1999-MI752	A	19990413		
	WO 2000-EP3239	W	20000411		

OS MARPAT 133:309791

AB Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

L2 ANSWER 68 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:742053 CAPLUS

DN 133:310142

TI Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

IN Del Soldato, Piero

PA Nicox S.A., Fr.

SO PCT Int. Appl., 159 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000061537	A2	20001019	WO 2000-EP3234	20000411
	WO 2000061537	A3	20010927		
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 1311924	B1	20020320	IT 1999-MI753	19990413
	CA 2370412	AA	20001019	CA 2000-2370412	20000411
	BR 2000009702	A	20020108	BR 2000-9702	20000411
	EP 1169294	A2	20020109	EP 2000-925203	20000411
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002541233	T2	20021203	JP 2000-610814	20000411
	NZ 514267	A	20040625	NZ 2000-514267	20000411
	RU 2237657	C2	20041010	RU 2001-127576	20000411
	AU 778989	B2	20041223	AU 2000-44001	20000411
	ZA 2001008127	A	20030103	ZA 2001-8127	20011003
	NO 2001004927	A	20011213	NO 2001-4927	20011010
	US 6869974	B1	20050322	US 2001-926326	20011015
PRAI	IT 1999-MI753	A	19990413		
	WO 2000-EP3234	W	20000411		

OS MARPAT 133:310142

AB Compds. A-B-C-N(O)s and A-C1[N(O)s]-B1 or their salts [s is an integer 1 or 2, preferably s = 2; A is the radical of a drug and is such as to meet the pharmacol. tests reported in the description; C and C1 are two bivalent radicals; the precursors of the radicals B and B1 are such as to meet the pharmacol. test reported in the description] were prepared for use as pharmaceuticals. Thus, (S,S)-N-acetyl-S-(6-methoxy- $\alpha$ -methyl-2-naphthalenylacetyl)cysteine 4-nitroxybutyl ester was prepared (NCX 2101) from naproxene and N-acetylcysteine in the first of 28 synthetic examples given. Pharmacol. test examples and tabular data are also given.

L2 ANSWER 69 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:668782 CAPLUS

DN 134:157218

TI Non-absorbable antibiotics for managing intestinal gas production and gas-related symptoms

AU Di Stefano, M.; Strocchi, A.; Malservisi, S.; Veneto, G.; Ferrieri, A.; Corazza, G. R.

CS Gastroenterology Unit, University of Pavia, Pavia, Italy

SO Alimentary Pharmacology and Therapeutics (2000), 14(8), 1001-1008

CODEN: APTHEN; ISSN: 0269-2813

PB Blackwell Science Ltd.

DT Journal

LA English

AB Simethicone, activated charcoal and antimicrobial drugs have been used to treat gas-related symptoms with conflicting results. The aim of this paper was to study the relationship between gaseous symptoms and colonic gas production and to test the efficacy of rifaximin, a new non-absorbable antimicrobial agent, on these symptoms. Intestinal gas production was measured by hydrogen (H<sub>2</sub>) and methane (CH<sub>4</sub>) breath testing after lactulose in 21 healthy volunteers and 34 functional patients. Only the 34 functional patients took part in a double-blind, double-dummy controlled trial, receiving, at random, rifaximin (400 mg b.d per 7 days), or activated charcoal (400 mg b.d per 7 days). The following parameters were evaluated at the start of the study and 1 and 10 days after therapy: bloating, abdominal pain, number of flatus episodes, abdominal girth, and cumulative breath H<sub>2</sub> excretion. Hydrogen excretion was greater in functional patients than in healthy volunteers. Rifaximin, but not activated charcoal, led to a significant reduction in H<sub>2</sub> excretion and overall severity of symptoms. In particular, in patients treated with rifaximin, a significant reduction in the mean number of flatus episodes and of mean abdominal girth was evident. In patients with gas-related symptoms the colonic production of H<sub>2</sub> is increased. Rifaximin significantly reduces this production and the excessive number of flatus episodes.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 70 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:530246 CAPLUS

DN 133:114632

TI In vitro activity and fecal concentration of rifaximin after oral administration

AU Jiang, Zhi-Dong; Ke, Shi; Palazzini, Ernesto; Riopel, Lise; Dupont, Herbert

CS Center for Infectious Disease, School of Public Health and Medical School, University of Texas-Houston, Houston, TX, USA

SO Antimicrobial Agents and Chemotherapy (2000), 44(8), 2205-2206  
CODEN: AMACCQ; ISSN: 0066-4804

PB American Society for Microbiology

DT Journal

LA English

AB Rifaximin showed moderately high MICs (the MIC at which 90% of the isolates tested were inhibited = 50 µg/mL) for 145 bacterial enteropathogens from patients with traveler's diarrhea acquired in Mexico during the summers of 1997 and 1998. Rifaximin concns. in stool the day after oral administration (800 mg daily for 3 days) were high (average, 7,961 µg/g), proving the value of the drug.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 71 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:494311 CAPLUS

DN 133:220067

TI In vitro activity of rifaximin, metronidazole and vancomycin against *Clostridium difficile* and the rate of selection of spontaneously resistant mutants against representative anaerobic and aerobic bacteria, including ammonia-producing species

AU Marchese, Anna; Salerno, Angelo; Pesce, Adelaide; Debbia, Eugenio A.; Schito, Gian Carlo

CS Istituto di Microbiologia "C.A. Romanzi", Universita di Genova, Genoa, I-16132, Italy

SO Chemotherapy (Basel) (2000), 46(4), 253-266

CODEN: CHTHBK; ISSN: 0009-3157

PB S. Karger AG

DT Journal

LA English

AB Rifaximin is a rifamycin derivative characterized by a wide antibacterial activity. This drug is neither absorbed by the gastrointestinal tract nor inactivated by gastric juices, and exerts its action entirely within the intestinal lumen. In this study, the activity of this antibiotic was compared with that of metronidazole and vancomycin against 93 *Clostridium difficile* isolates. The rate of emergence of bacteria spontaneously resistant to the new compound was also evaluated in relation to representative gram-pos. and gram-neg. strains. In terms of MIC50 values, rifaximin showed an intrinsic activity superior to that of the other agents. The emergence of spontaneously resistant strains was assessed with 46 aerobic (staphylococci, enterococci, *Proteus* spp., *Citrobacter freundii*, *Providencia rettgeri*, enteropathogenic, enteroinvasive, enterotoxigenic and enterohemorrhagic *Escherichia coli*, and *Salmonella enteritidis*) and anaerobic (*Clostridium* spp., *Bacteroides* spp., *Fusobacterium nucleatum* and *Peptococcus* spp.) pathogens, most of them also ammonium producers. Two different methods, broth and agar dilution, were employed. When liquid medium was employed, bacteria capable of sustained growth in 100 µg/mL of rifaximin were obtained after 2-5 transfers with gram-pos. aerobic cocci, 2-3 transfers with gram-neg. aerobic strains and 2-5 transfers with anaerobic species. At the highest dose used with the agar dilution method (8 + MIC), the frequency of emergence of spontaneously resistant mutants ranged from  $<1 + 10^{-9}$  to  $1.6 + 10^{-8}$  with gram-pos. aerobic and anaerobic cocci, while with aerobic and anaerobic gram-neg. bacteria, this value ranged from  $<1 + 10^{-9}$  to  $1.7 + 10^{-7}$ . *C. difficile* showed a particularly low incidence of spontaneously resistant mutants ( $<1 + 10^{-9}$ ). The low incidence of resistant subpopulations selected by levels of 8 + MIC of rifaximin suggests that the high levels of the drug which were reached in the gastrointestinal lumen may further prevent the selection of mutants. The low toxicity, broad antibacterial activity and very poor absorption from the gastrointestinal tract of rifaximin suggest a potential therapeutic use for this drug in gastrointestinal diseases, as well as in the management of patients with cirrhosis and chronic portal-systemic encephalopathy.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



L2 ANSWER 72 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:390317 CAPLUS

DN 133:12378

TI Rifaximin versus chlortetracycline in the short-term treatment of small intestinal bacterial overgrowth

AU Di Stefano, M.; Malservisi, S.; Veneto, G.; Ferrieri, A.; Corazza, G. R.

CS Gastroenterology Unit. IRCCS "S. Matteo" Hospital, University of Pavia, Pavia, 27100, Italy

SO Alimentary Pharmacology and Therapeutics (2000), 14(5), 551-556

CODEN: APTHEN; ISSN: 0269-2813

PB Blackwell Science Ltd.

DT Journal

LA English

AB Bacterial overgrowth of the small intestine is a condition characterized by nutrient malabsorption due to an excessive number of bacteria in the lumen of the small intestine. Current treatment is based on empirical courses of broad spectrum antibiotics: few controlled data, with respect to the duration and choice of antibiotic drug, exist at present. The recent availability of rifaximin, a non-absorbable rifamycin derivative, highly effective against anaerobic bacteria, prompted us to carry out a randomized, double-blind controlled trial in order to compare its efficacy and tolerability to those of tetracycline, currently considered the first-choice drug. In 21 patients affected by small intestinal bacterial overgrowth, fasting, peak and total H<sub>2</sub> excretion after ingestion of 50 g glucose and severity of symptoms were evaluated before and after a 7-day course of rifaximin, 1200 mg/day (400 mg t.d.s.), or chlortetracycline, 1 g/day (333 mg t.d.s.). Fasting, peak and total H<sub>2</sub> excretion decreased significantly in the group of patients treated with rifaximin whereas chlortetracycline did not modify these parameters. The H<sub>2</sub> breath test normalized in 70% of patients after rifaximin and in 27% of patients after chlortetracycline. The improvement in symptoms was significantly higher in patients treated with rifaximin. Rifaximin is a promising, easily-handled and safe drug for the short-term treatment of small intestinal bacterial overgrowth.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 73 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:228871 CAPLUS

DN 132:231564

TI Evaluation of the efficacy and safety of rifaximin in the treatment of hepatic encephalopathy: a double-blind, randomized, dose-finding multi-centre study

AU Williams, Roger; James, Oliver F. W.; Warnes, Thomas W.; Morgan, Marsha Y.

CS Liver Research Unit, King's College Hospital, London, UK

SO European Journal of Gastroenterology & Hepatology (2000), 12(2), 203-208

CODEN: EJGHES; ISSN: 0954-691X

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB The aim of this study was to determine the efficacy, tolerability and safety of oral rifaximin given at three dose levels in patients with cirrhosis and mild to moderate hepatic encephalopathy (HE). This was a prospective, double-blind, randomized, parallel-group study. Setting was a multi-center trial in four university teaching hospitals. Patients were fifty-four patients with cirrhosis and mild to moderate HE. Seven days treatment with rifaximin, 600, 1200 or 2400 mg/day in three divided doses. Main outcome measure Change in the portal-systemic encephalopathy (PSE) index between baseline and day 7, calculated on the basis of mental state, asterixis, number connection test time, EEG mean cycle frequency and blood ammonia concns. Treatment with rifaximin was associated with an improvement in the PSE index. There was a trend towards a greater treatment effect of rifaximin with the highest dose of 2400 mg/day. Rifaximin was well tolerated; the few treatment-related adverse events showed no consistent pattern or dose relationship. Rifaximin may be useful as alternative or adjuvant therapy for grade I-III hepatic encephalopathy in patients with cirrhosis at a dose of 1200 mg/day.

L2 ANSWER 74 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:183425 CAPLUS

DN 132:202689

TI Effect of rifaximin on intestinal bacterial overgrowth in Crohn's disease as assessed by the H<sub>2</sub>-glucose breath test

AU Biancone, L.; Vernia, P.; Agostini, D.; Ferrieri, A.; Pallone, F.

CS Istituto di Clinica Medica 2, Universita "La Sapienza", Rome, Italy

SO Current Medical Research and Opinion (2000), 16(1), 14-20

CODEN: CMROCX; ISSN: 0300-7995

PB LibraPharm Ltd.

DT Journal

LA English

AB The occurrence of intestinal bacterial overgrowth in patients with Crohn's Disease (CD) has been described and antimicrobial treatment has been shown to be effective in reversing this condition. However, the mechanisms underlying the efficacy of antimicrobial therapy are still only partially known. The aim of the present study was to evaluate the effect of a non-absorbable antibiotic (rifaximin) in comparison to placebo on bacterial overgrowth in patients with CD. Methods: Fourteen patients with inactive CD of the ileum and bacterial overgrowth, as assessed by the hydrogen breath test, were blindly allocated to receive rifaximin (1200 mg/day) or placebo t.i.d. for one week. A hydrogen breath test, and clin. and biochem. parameters were further performed 14 days and 30 days after starting treatment. Results: After 14 days, the hydrogen breath test proved to be neg. in seven out of seven patients treated with rifaximin ( $p < 0.05$ ), and in two out of seven in the placebo group ( $p = ns$ ). After 30 days, the hydrogen breath test was pos. in all patients of the rifaximin and placebo group, resp. No changes in the CDAI score were documented in any patients. Conclusions: Short-term administration of rifaximin is effective in the therapy of bacterial overgrowth in patients with inactive CD of the ileum, thus suggesting that the control of luminal bacterial growth could be useful in the management of these patients. However, since we observed a decline with time in this pos. effect, further studies are needed to identify the most appropriate therapeutic strategies.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 75 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:442847 CAPLUS

DN 131:138963

TI Antibiotic combination therapy in patients with chronic, treatment-resistant pouchitis

AU Gionchetti, P.; Rizzello, F.; Venturi, A.; Ugolini, F.; Rossi, M.; Brigidi, P.; Johansson, R.; Ferrieri, A.; Poggioli, G.; Campieri, M.

CS Dipartimento di Medicina Interna e Gastroenterologia, Bologna, 9-40138, Italy

SO Alimentary Pharmacology and Therapeutics (1999), 13(6), 713-718  
CODEN: APTHEN; ISSN: 0269-2813

PB Blackwell Science Ltd.

DT Journal

LA English

AB Pouchitis is the major long-term complication after ileal pouch-anal anastomosis for ulcerative colitis. About 15% of patients have a chronic, treatment-resistant disease. To evaluate the efficacy of an antibiotic combination for chronic active, treatment-resistant pouchitis. Eighteen patients were treated orally with rifaximin 1 g b.d. + ciprofloxacin 500 mg b.d. for 15 days. Symptoms assessment, endoscopic and histol. evaluations were performed at screening and after 15 days using the Pouchitis Disease Activity Index (PDAI). Improvement was defined as a decrease of at least 3 points in PDAI score, and remission as a PDAI score of 0. Systemic absorption of rifaximin was determined by high performance

liquid

chromatog. Faecal samples were collected before and after antibiotic treatment for stool culture. Sixteen out of 18 patients (88.8%) either improved (n=10) or went into remission (n=6); the median PDAI scores before and after therapy were 11 (range 9-17) and 4 (range 0-16), resp. ( $P < 0.002$ ). No side-effects were reported. Rifaximin plasma levels and urinary excretion were negligible, confirming its mainly topical activity. A significant decrease in total anaerobes and aerobes, enterococci, lactobacilli, bifidobacteria and bacteroides in fecal samples was observed, while the reduction in number of coliforms and *Clostridium perfringens* did not reach a statistical significance. A combination of rifaximin and ciprofloxacin was effective in patients with active chronic, treatment-resistant pouchitis, suggesting the need, in these patients, for treatment using antibiotic agents with wide antibacterial spectrum of activity.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 76 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:436273 CAPLUS

DN 131:110931

TI Rifaximin in patients with moderate or severe ulcerative colitis  
refractory to steroid treatment: A double-blind, placebo-controlled trial

AU Gionchetti, P.; Rizzello, F.; Ferrieri, A.; Venturi, A.; Brignola, C.;  
Ferretti, M.; Peruzzo, S.; Miglioli, M.; Campieri, M.

CS Department of Internal Medicine and Gastroenterology, S. Orsola Hospital,  
University of Bologna, Bologna, 40128, Italy

SO Digestive Diseases and Sciences (1999), 44(6), 1220-1221

CODEN: DDSCDJ; ISSN: 0163-2116

PB Kluwer Academic/Plenum Publishers

DT Journal

LA English

AB Rifaximin (200 mg twice daily, orally, for 10 days) appeared to be useful  
in patients with severe ulcerative colitis unresponsive to corticosteroid  
treatment. Although there was no significant difference in total clin.  
outcome between rifaximin-treated and placebo-treated patients, rifaximin  
reduced stool frequency, rectal bleeding, and sigmoidoscopic findings.  
Rifaximin was safe, well tolerated, and virtually nonabsorbed orally,  
confirming its mainly topical antibacterial activity.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 77 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:776740 CAPLUS

DN 130:20251

TI Rifaximin. A nonabsorbed antimicrobial in the therapy of travelers' diarrhea

AU DuPont, Herbert L.; Ericsson, C. D.; Mathewson, J. J.; Palazzini, E.; DuPont, M. W.; Jiang, Z. D.; Mosavi, A.; De la Cabada, F. J.

CS St. Luke's Episcopal Hospital, Houston, TX, 77030, USA

SO Digestion (1998), 59(6), 708-714

CODEN: DIGEBW; ISSN: 0012-2823

PB S. Karger AG

DT Journal

LA English

AB Bacterial enteropathogens, the major cause of travelers' diarrhea, are customarily treated with antibacterial drugs. Rifaximin, a non-absorbed antimicrobial was examined as treatment for travelers' diarrhea. A randomized, prospective, double-blind clin. trial was carried out in 72 US adults in Mexico. Patients with acute diarrhea received 1 of 3 doses of rifaximin (200, 400, and 600 mg t.i.d.) or trimethoprim/sulfamethoxazole (TMP/SMX, 160 mg/800 mg b.i.d.) for 5 days. Results were compared with data from 2 placebo-treated historical control populations. The shortest duration of treated diarrhea was seen in the group receiving 200 mg rifaximin t.i.d (NS). Clin. failure to respond to treatment occurred in 6/55 (11%) rifaximin-treated subjects vs. 5/17 (29%) of TMP/SMX-treated subjects (NS). 16/20 (80%) Of the enteropathogens isolated from the rifaximin-treated subjects and 7/7 (100%) from the TMP/SMX group were eradicated by treatment (NS). 16/24 (67%) Enteropathogens identified were susceptible to TMP and all 24 were inhibited by  $\leq 50$   $\mu\text{g/mL}$  of rifaximin. Rifaximin reduced the number of unformed stools passed during the 1st 24 h of treatment when compared with 2 control placebo groups (3.3 vs. 5.1) and led to a reduced duration of post-enrollment diarrhea (mean values of 43.1 vs. 68.1 and 81.9 h). Rifaximin shortened the duration of travelers' diarrhea compared with TMP/SMX and 2 earlier studied placebo-treated groups. A poorly absorbed drug is effective in treating bacterial diarrhea has pharmacol. and safety advantages over the existing drugs.

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 78 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:730938 CAPLUS

DN 130:104834

TI Rifaximin treatment for acute recurrent diarrhea in children with genitourinary disorders

AU De Castro, Roberto; Domenichelli, Vincenzo; Di Lorenzo, Francesco Paolo; Prestipino, Marco; Perrotta, Maria Luisa

CS Department of Paediatric Surgery, Policlinic "St. Orsola-Malpighi," Medical Department, University of Bologna, Bologna, 9-40138, Italy

SO Current Therapeutic Research (1998), 59(10), 746-752

CODEN: CTCEA9; ISSN: 0011-393X

PB Excerpta Medica

DT Journal

LA English

AB This study was undertaken to investigate the suitability of rifaximin for short-term treatment of acute bacterial diarrhea in children receiving long-term prophylactic therapy for urinary tract infections. Using a 2:1 ratio, 46 children (mean age, 4.9 yr) were consecutively assigned to receive either rifaximin oral suspension (n = 30) or oral rehydration (control group, n = 16) for a maximum of 5 days. After 5 days, in the rifaximin groups, 15 patients (50.0%) were clin. cured, 13 (43.3%) improved, and 2 (6.7%) had an insufficient outcome. In the control group, 5 patients (31.2%) were clin. cured after 4 days, 2 patients (12.5%) improved after 5 days, 4 (25.0%) had a sufficient outcome, and 5 (31.2%) had an insufficient outcome. Stools normalized rapidly during treatment with rifaximin-formed stools were detected in 24 children (80.0%) on treatment day 1. Only 2 patients still had watery stools after 5 days of treatment. In the control group, patients' stools normalized after 4 days in 7 children (43.8%) and after 5 days in 2 (12.5%); stools had not normalized by the end of the 5-day period in the remaining 7 patients (43.8%). Overall, a quick and statistically significant remission of fever and other clin. symptoms was seen with rifaximin. In the control group, symptoms were reduced more slowly. No adverse events, withdrawals, or dropouts occurred in the rifaximin group. The rapidity, effectiveness, and safety of rifaximin suggest that it is suitable for the treatment of acute recurrent episodes of diarrhea in children periodically undergoing prophylactic therapy for other genitourinary pathol. conditions.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 79 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1998:568600 CAPLUS  
DN 129:156922  
TI Use of rifaximin in treatment of diarrhea from cryptosporidiosis  
PA Alfa Wassermann S.P.A., Italy  
SO Eur. Pat. Appl., 5 pp.  
CODEN: EPXXDW

DT Patent  
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 858804	A1	19980819	EP 1998-101081	19980122
	EP 858804	B1	20020605		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	AT 218342	E	20020615	AT 1998-101081	19980122
	PT 858804	T	20021031	PT 1998-101081	19980122
	ES 2178048	T3	20021216	ES 1998-101081	19980122
	US 5886002	A	19990323	US 1998-13655	19980126
	JP 10226645	A2	19980825	JP 1998-29813	19980212
	CN 1214244	A	19990421	CN 1998-106920	19980213
	CN 1115146	B	20030723		
PRAI	IT 1997-BO64	A	19970214		

AB Rifaximin and pharmaceutical compns. containing it are useful in treatment of the diarrheal symptomatol. in cryptosporidiosis in patients suffering from severe forms of immunodepression, e.g. in patients suffering from AIDS or malignant neoplasias, or subjected to transplantation or treatment with chemotherapeutic or immunosuppressive agents. Thus, AIDS patients with secondary diarrhea caused by Cryptosporidium parvum infection and severe immunodepression were administered rifaximin (3 + 200 mg 3 times a day orally for 10-21 days). At the end of treatment, Cryptosporidium oocysts had disappeared from the feces in 7 of 12 patients, and the diarrheal symptomatol. disappeared or improved in 10 patients, with no adverse side effects.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



10/728,090

L2 ANSWER 80 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:194963 CAPLUS

DN 129:36067

TI Rifaximin systemic absorption in patients with ulcerative colitis

AU Rizzello, F.; Gionchetti, P.; Venturi, A.; Ferretti, M.; Peruzzo, S.;  
Raspanti, X.; Picard, M.; Canova, N.; Palazzini, E.; Campieri, M.

CS Medical Dept. Alfa Wassermann SpA, Via Ragazzi del '99, Bologna, 40133,  
Italy

SO European Journal of Clinical Pharmacology (1998), 54(1), 91-93

CODEN: EJCPAS; ISSN: 0031-6970

PB Springer-Verlag

DT Journal

LA English

AB HPLC was used to determine rifaximin in the plasma and urine of patients with ulcerative colitis who received a single oral 400-mg dose of the drug. Rifaximin was detectable in the plasma of only a few patients during the 1st 8 h after administration, and only minor amts. were found in urine. There was no correlation between disease severity and the plasma or urinary drug concns. The mean total amount of drug excreted in the urine of these patients in the 1st 24 h after administration was similar to that previously reported for healthy persons. The data suggest the virtual absence of absorption of rifaximin, and hence negligible passage into the general circulation.

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/728,090

L2 ANSWER 81 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:105015 CAPLUS

DN 128:212762

TI An open, controlled study of two non-absorbable antibiotics for the oral treatment of pediatric infectious diarrhea

AU Frisari, L.; Viggiano, V.; Pelagalli, M.

CS Paediatric Surgery Department, "C. A. Pizzardi" Hospital, Bologna, 40100, Italy

SO Current Medical Research and Opinion (1997), 14(1), 39-45  
CODEN: CMROCX; ISSN: 0300-7995

PB LibraPharm

DT Journal

LA English

AB Forty-nine children in need of antibacterial treatment for a severe episode of bacterial diarrhea were consecutively treated with either an oral pediatric suspension of rifaximin (100 mg every six hours for an average of four days: 24 patients), or paromomycin (125 mg every six hours for an average of four days: 25 patients). Stools (number and form), enteritis symptoms

and signs, and intolerance manifestations were all monitored on each day of treatment. A stool culture was performed on the first available stool after enrollment and after the end of treatment to monitor the drugs' antibacterial activity. A similar rate of bacteriol. cure, with normalization of stools and elimination of the clin. symptomatol., was attained by the two antibiotics, with statistical significance of changes vs. baseline being apparent on the second treatment day, in both treatment groups. Rifaximin results were quicker (treatment lasted three days in several cases) and on the whole slightly better (though without statistical significance) than those of paromomycin: 21/24 vs. 20/25 children were completely cured, with a failure rate of three and five cases, resp. Systemic and local tolerance of both treatments were very good in all children.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 82 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:87332 CAPLUS

DN 128:200829

TI Antibacterial activity of rifaximin reduces the levels of  
benzodiazepine-like compounds in patients with liver cirrhosis

AU Zeneroli, M. L.; Venturini, I.; Stefanelli, S.; Farina, F.; Miglioli, R.  
Cosenza L.; Minelli, E.; Amedei, R.; Ferrieri, A.; Avallone, R.; Baraldi,  
M.

CS Cattedra di Semeiotica e Metodologia Medica, Universita di Modena,  
Bologna, Italy

SO Pharmacological Research (1997), 35(6), 557-560

CODEN: PHMREP; ISSN: 1043-6618

PB Academic Press Ltd.

DT Journal

LA English

AB Benzodiazepine-like compds. are present in trace amts. in the blood of  
normal subjects and increase in liver cirrhotic patients with or without  
encephalopathy. Their increased presence may, however, represent an  
occasional precipitating factor of hepatic encephalopathy. The source of these  
compds. is still unknown, but they are constituents of our diet, since  
benzodiazepine receptor ligands have been described in plants, vegetables  
and in animals. They may also be synthesized, at least in part, by  
intestinal bacterial flora. The authors report that the level of these  
compds. in the blood decreased by 40% after therapy with rifaximin, which  
reduces the aerobic and anaerobic intestinal bacterial flora. This  
observation indicates that intestinal bacterial flora is involved in the  
production of these compds. and that repeated short-term medications with this  
non-absorbable antibiotic may be useful in reducing the levels of  
benzodiazepine-like compds. in patients with liver cirrhosis.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 83 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:624819 CAPLUS

DN 127:272308

TI Rifaximin, a non-absorbable rifamycin, for the treatment of hepatic encephalopathy. A double-blind, randomized trial

AU Miglio, Federico; Valpiani, Daniela; Rossellini, Salvatore Ricca; Ferrieri, Antonella

CS Service of First Aid and Emergency Medicine, St Orsola Hospital, Bologna, Italy

SO Current Medical Research and Opinion (1997), 13(10), 593-601  
CODEN: CMROCX; ISSN: 0300-7995

PB LibraPharm

DT Journal

LA English

AB The aim of this study was to evaluate the efficacy and tolerability of rifaximin, a non-absorbable intestinal antibiotic, in comparison to neomycin in the short- and long-term treatment of hepatic encephalopathy (HE). Forty-nine patients with a definite diagnosis of cirrhosis were included in this double-blind, randomized, controlled trial. Patients were randomly assigned to one of the following treatments: (1) rifaximin 400 mg three times daily; (2) neomycin 1 g three times daily. Both drugs were administered orally as tablets during 14 consecutive days each month, for a period of six months. The neuropsychiatric signs and blood ammonia levels were examined before starting the treatment, and every 30 days, until the final assessment. In all patients a progressive and important reduction in HE grade was observed, and no statistically significant difference between the two treatments was detected. In both groups the disturbances in speech, memory, behavior and mood, gait, asterixis, writing, and serial subtraction of 7 s and five-pointed star tests all showed the highest proportion of improvement. During the study blood ammonia levels decreased in both the rifaximin and in the neomycin groups, and again no statistically significant difference was found between groups. Our findings confirm, therefore, the usefulness of rifaximin in the treatment of HE, supporting its use as a first-choice antibiotic, particularly in patients intolerant to neomycin or with impaired renal function.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 84 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:399311 CAPLUS

DN 127:75584

TI Rifaximin suspension for the eradication of *Helicobacter pylori*

AU Vaira, Dino; Menegatti, Marcello; Miglioli, Mario; Ferrieri, Antonella; Holton, John; Biasco, Guido; Azzarone, Pasquale; Ricci, Chiara; Gusmaroli, Riccardo; et al.

CS First Medical Clinic, University of Bologna, Bologna, Italy

SO Current Therapeutic Research (1997), 58(5), 300-308

CODEN: CTCEA9; ISSN: 0011-393X

PB Excerpta Medica

DT Journal

LA English

AB The in vitro sensitivity of *Helicobacter pylori* to rifaximin, a new rifamycin antibiotic, was evaluated in 40 clin. isolates by the agar dilution method. Rifaximin showed good activity, with a 50% min. inhibitory concentration

of 4 mg/L-1. Consequently, we assessed rifaximin in *H pylori*-pos. patients. Overall, 71 patients with upper gastrointestinal symptoms (35 men and 36 women; aged 19 to 73 yr, mean, 45.6 yr) were found to have *H pylori*-associated gastritis. The first 30 consecutive patients received monotherapy with rifaximin 600 mg three times a day (TID) for 14 days. The 41 patients enrolled thereafter were allocated in an open, randomized fashion to four different treatment groups for 14 days: (1) rifaximin 600 mg TID and colloidal bismuth subcitrate 240 mg twice a day (BID) (n = 10); (2) rifaximin 600 mg TID and omeprazole 20 mg BID (n = 10); (3) rifaximin 600 mg TID and amoxicillin 1 g BID (n = 10); or (4) rifaximin 1800 mg TID and metronidazole 500 mg TID (n = 11). Upper gastrointestinal symptoms (pyrosis, bloating, epigastric pain, and nausea) were recorded and assessed before and 4 wk after treatment. Patients were assessed by endoscopy, histol., CP test, culture, and serol. (IgG [IgG] to *H pylori*) at entry. Sixty-seven patients were available for follow-up 4 wk after the completion of treatment. A statistically significant improvement in symptoms was seen in patients treated with rifaximin and rifaximin plus colloidal bismuth subcitrate. No statistically significant differences in degree of improvement in endoscopic and histol. findings were seen among the five treatment groups. A statistically significant decrease in the mean IgG value after treatment was found for rifaximin, rifaximin plus colloidal bismuth subcitrate, and rifaximin plus omeprazole. The overall eradication rate was 43%. These results suggest that rifaximin may be an effective antibiotic against *H pylori* infection and is worthy of further study.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 85 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1997:203083 CAPLUS  
DN 126:197310  
TI Selection of rifampicin-resistant Mycobacterium tuberculosis does not  
occur in the presence of low concentrations of rifaximin  
AU Soro, Ornella; Pesce, Adelaide; Raggi, Monica; Debbia, Eugenio A.; Schito,  
Gian Carlo  
CS Institute of Microbiology, School of Medicine, University of Genoa, Genoa,  
16132, Italy  
SO Clinical Microbiology and Infection (1997), 3(1), 147-151  
CODEN: CMINFM; ISSN: 1198-743X  
PB Decker Europe  
DT Journal  
LA English  
AB Under the studied test conditions, no Mycobacterium tuberculosis pathogens  
resistant to both rifampicin and rifaximin were selected. As the  
rifaximin concns. used were higher than those expected from intestinal  
absorption, it is probable that the min. amts. of rifaximin possibly  
resorbed into the systemic fluids after oral administration do not  
represent a level which will induce the selection of drug-resistant  
microorganisms.

L2 ANSWER 86 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:685021 CAPLUS

DN 126:84128

TI Bacterial translocation in the course of acute pancreatitis. Beneficial role of nonabsorbable antibiotics and lactitol enemas

AU Marotta, Francesco; Geng, T. C.; Wu, C. C.; Barbi, G.

CS Department Internal Medicine, S. Anna Hospital, Como, Italy

SO Digestion (1996), 57(6), 446-452

CODEN: DIGEBW; ISSN: 0012-2823

PB Karger

DT Journal

LA English

AB To study the bacterial translocation in the course of acute pancreatitis, rats with acute pancreatitis induced by intrabiliary injection of a trypsin/enterokinase mixture were treated as follows: group A no treatment, group B given a daily 30 mL enema with 20 mg/kg rifaximin, group C given a daily 30 mL enema with 20 mg/kg rifaximin plus lactitol 0.5 g/kg, and group D given a daily 30 mL enema with warm saline. A group of healthy rats was given an intrabiliary injection of 0.15 mL saline. Both enema treatments brought about an improvement in survival. A time-course increase in endotoxin level was observed in untreated rats. Decreased levels were observed after both enema treatments. Ascites was the sample most frequently infected. Lymph nodes contiguous to the gut were infected more frequently than those close to major vessels. The histol. pancreatic damage was to lesser degree in both enema treatment groups. Virtually all severe necrotic-hemorrhagic pancreatic lesions were associated with bacterial infection. Bacterial translocation plays a relevant role in the outcome of exptl. necrotizing pancreatitis. Intra-abdominal spread and lymphatics seem to be the pathways most likely involved in such processes. Colonic cleansing by non-absorbable antibiotics and lactitol seems to exert a beneficial effect on the supervening infection.

10/728,090

L2 ANSWER 87 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1996:651055 CAPLUS  
DN 126:103940  
TI NMR investigation of a new semisynthetic bioactive compound  
AU Rossi, Claudio; Donati, Alessandro; Renzoni, Debora; Bonechi, Claudia;  
Marchettini, Nadia  
CS Department Chemistry, University Siena, Siena, 53100, Italy  
SO Bulletin of Magnetic Resonance (1996), 18(1/2), 87-90  
CODEN: BUMRDT; ISSN: 0163-559X  
PB International Society of Magnetic Resonance  
DT Journal  
LA English  
AB The <sup>1</sup>H NMR and NOESY determined the solution structure of the ansamycin  
derivative,  
rifaximin OR (ring opened), obtained in the electroredn. of rifaximin.  
The NMR structure agreed with the mol. mech. calcn.



10/728,090

L2 ANSWER 88 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1996:409094 CAPLUS  
DN 125:142388  
TI NMR studies of a new class of rifaximin-derived molecules: rifaximin OR  
(open ring)  
AU Rossi, Claudio; Marchettini, Nadia; Bonechi, Claudia; Donati, Alessandro;  
Corbini, Gianfranco; Corti, Piero  
CS Dep. Chem., Univ. Siena, Siena, 53100, Italy  
SO Journal of Chemical Research, Synopses (1996), (6), 268-269  
CODEN: JRPSDC; ISSN: 0308-2342  
PB Royal Society of Chemistry  
DT Journal  
LA English  
AB The electrolytic selective reduction of the aliphatic chain of rifaximin gave a  
new open-ring ansamycin structure which has been characterized by NMR  
spectroscopy.

L2 ANSWER 89 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:533728 CAPLUS

DN 122:281136

TI Rifaximin: A review of its antibacterial activity, pharmacokinetic properties and therapeutic potential in conditions mediated by gastrointestinal bacteria

AU Gillis, Jane C.; Brogden, Rex N.

CS Adis International Limited, Auckland, N. Z.

SO Drugs (1995), 49(3), 467-84

CODEN: DRUGAY; ISSN: 0012-6667

DT Journal; General Review

LA English

AB A review with 66 refs. Rifaximin is a derivative of rifamycin which acts by inhibiting bacterial RNA (RNA) synthesis. It is virtually unabsorbed after oral administration; thus it is used primarily to treat local conditions within the gastrointestinal tract. In vitro data indicate rifaximin possesses good activity against species of Staphylococcus, Streptococcus and Enterococcus but lesser activity against species of Enterobacteriaceae. Bacterial resistance during exposure to rifaximin has been reported but its clin. importance remains to be fully defined. Results of comparative trials demonstrate that rifaximin is similar in efficacy to neomycin and lactulose in patients with hepatic encephalopathy and appears to be better tolerated. In 1 study, cyclical administration of rifaximin for 15 days per mo was associated with progressive improvement over a 3-mo period. In patients with infectious diarrhea, rifaximin induces more rapid improvement in stool consistency and decreased frequency of fecal evacuations when compared with placebo, and is similar in efficacy to neomycin. Available data suggest rifaximin may be of some use in acute diverticulitis, but its use for the prevention of inflammatory complications or for control of common symptoms of diverticulosis requires further study. Preoperative treatment with rifaximin as antibacterial prophylaxis in colorectal surgery shows some potential but should be further investigated. Overall, rifaximin may be useful as an alternative therapy in hepatic encephalopathy but more data are needed to better define its clin. potential in infectious diarrhoea, diverticular disease and as antibacterial prophylaxis prior to colorectal surgery.

10/728,090

L2 ANSWER 90 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:525212 CAPLUS

DN 122:286425

TI The susceptibility of *Helicobacter pylori* to the rifamycin, rifaximin

AU Holton, J.; Vaira, D.; Menegatti, M.; Barbara, L.

CS Dep. Med. Microbiol., Univ. Coll. London Med. Sch., London, W1P 7PN, UK

SO Journal of Antimicrobial Chemotherapy (1995), 35(4), 545-9

CODEN: JACHDX; ISSN: 0305-7453

PB Saunders

DT Journal

LA English

AB Forty strains of *Helicobacter pylori* had an MIC50 of 4 mg/L of the non-absorbable antibiotic, rifaximin. Neither synergy nor antagonism was demonstrated when the drug was combined with ampicillin, metronidazole and omeprazole and the rate of spontaneous mutation was less than 1 in 108. With these in-vitro characteristics, rifaximin should now be assessed for clin. efficacy.

L2 ANSWER 91 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1994:691948 CAPLUS

DN 121:291948

TI Pharmacokinetic study of rifaximin after oral administration in healthy volunteers

AU Descombe, J.J.; Dubourg, D.; Picard, M.; Palazzini, E.

CS Laboratoire de Recherche pour l'Industrie du Medicament, Larime S.A., Lagord, Fr.

SO International Journal of Clinical Pharmacology Research (1994), 14(2), 51-6

CODEN: CPHRDE; ISSN: 0251-1649

PB Bioscience Ediprint

DT Journal

LA English

AB Healthy male volunteers, with a mean age of 24 yr (range 18-40), underwent an open pharmacokinetics study, aimed at detecting rifaximin concentration in blood and urine after a single oral administration of 400 mg of the antibiotic. Administration took place after a 9-h fast and was followed by a breakfast after 2 h and a lunch after 5 h. Blood samples were collected before rifaximin administration and 1, 2, 4, 8, 12, 24 and 48 h thereafter. Urine samples were collected immediately before administration and then at the end of the following intervals of time: 0-6, 6-12, 12-24, 24-48 h. Rifaximin concentration was assessed by reversed phase HPLC with electrochem. detection. In almost every plasma sample, rifaximin concentration was undetectable (<2 ng/mL). In urine, very small

amts.

of the unchanged mol. (<0.01% of the administered dose) were found in the period 0-48 h. These results confirm the negligible absorption by the intestinal tract of a single oral dose of rifaximin (400 mg). Local and general tolerance of the administered drug was very good.

10/728,090

L2 ANSWER 92 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1994:646330 CAPLUS

DN 121:246330

TI Use of rifaximin for the treatment of gastric dyspepsia caused by  
Helicobacter pylori

IN Ferrieri, Antonella; Rotini, Leone Gabriele

PA Alfa Wassermann S.p.A., Italy

SO Eur. Pat. Appl., 7 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	EP 616808	A1	19940928	EP 1994-104308	19940318
	EP 616808	B1	19960911		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, LI, LU, NL, PT, SE				
	US 5352679	A	19941004	US 1993-83453	19930628
	CA 2115381	AA	19940924	CA 1994-2115381	19940210
	CA 2115381	C	19990105		
	KR 177846	B1	19990320	KR 1994-4654	19940310
	JP 06298768	A2	19941025	JP 1994-47045	19940317
	JP 2755550	B2	19980520		
	AT 142495	E	19960915	AT 1994-104308	19940318
	ES 2091649	T3	19961101	ES 1994-104308	19940318
PRAI	IT 1993-BO99	A	19930323		

AB Rifamycin antibiotic and pharmaceutical compns. containing it are used in the oral treatment of gastric dyspepsia caused by Helicobacter pylori. Patients affected with dyspeptic symptoms caused by gastritis due to Helicobacter pylori were treated orally with 188 mg/day rifaximin for 14 days. Endoscopic examination confirmed the disappearance of gastritis and considerable reduction of erosive lesions.

10/728,090

L2 ANSWER 93 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1994:553113 CAPLUS

DN 121:153113

TI In vitro activity of rifaximin against *Helicobacter pylori*

AU Megraud, F.; Bouffant, F.; Junras, C. Camou

CS Lab. Bacteriol., Univ. Bordeaux II, Bordeaux, F-33076, Fr.

SO European Journal of Clinical Microbiology & Infectious Diseases (1994),  
13(2), 184-6

CODEN: EJCDEU; ISSN: 0934-9723

DT Journal

LA English

AB The in vitro activity of rifaximin against the title organism and the acquisition of rifaximin resistance were determined. Rifaximin displayed an activity in the same MIC range as that of rifampicin (0.5-8 at pH 6). The strains tested became resistant after exposure to subinhibitory concns. of the antibiotic. The mutation frequency with rifaximin was in the range of that observed with macrolides and quinolones, but less frequent than that observed with metronidazole.

10/728,090

L2 ANSWER 94 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1993:480251 CAPLUS  
DN 119:80251  
TI Pharmaceutical compositions containing rifaximin for treatment of vaginal  
infections  
IN Marchi, Egidio; Rotini, Lene Gabriele; Desai, Subhash; Grilli, Massimo  
PA Alfa Wassermann S.P.A., Italy  
SO Eur. Pat. Appl., 14 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	EP 547294	A1	19930623	EP 1992-113603	19920810
	EP 547294	B1	19951122		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	US 5314904	A	19940524	US 1992-899421	19920616
	CA 2073601	AA	19930618	CA 1992-2073601	19920710
	CA 2073601	C	19960709		
	KR 149519	B1	19981015	KR 1992-12471	19920714
	AT 130510	E	19951215	AT 1992-113603	19920810
	ES 2081531	T3	19960301	ES 1992-113603	19920810
	JP 05255085	A2	19931005	JP 1992-266034	19921005
	JP 2834951	B2	19981214		
	US 6140355	A	20001031	US 1994-181259	19940113
PRAI	IT 1991-BO476	A	19911217		
	US 1992-899421	A3	19920616		

AB The title compns., e.g. vaginal foams, are useful in the treatment of vaginal infections. A vaginal foam contained rifaximin 200, cetyl stearyl alc. 160, mineral oil 3640, and a mixture of butane:propane:isobutane (55:25:20) 3150mg. Thus, 86.7% of women affected with bacterial vaginosis were treated by one application of the foam prior to going to bed for 5 consecutive nights.

10/728,090

L2 ANSWER 95 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1993:467858 CAPLUS

DN 119:67858

TI In vitro activity of rifaximin, a topical rifamycin derivative, against  
Chlamydia trachomatis

AU Prasad, Errol S.; Wenman, Wanda M.

CS Prov. Lab. Public Health North. Alberta, Univ. Alberta, Edmonton, AB, Can.

SO Diagnostic Microbiology and Infectious Disease (1993), 16(2), 135-6

CODEN: DMIDDZ; ISSN: 0732-8893

DT Journal

LA English

AB Rifaximin is a rifamycin derivative that possesses in vitro activity against a  
wide range of bacteria. Its antimicrobial spectrum plus poor intestinal  
absorption have led to consideration of this compound as a topical agent.  
The authors evaluated its in vitro activity against clin. and laboratory  
strains

of Chlamydia trachomatis and found that rifaximin exhibits min. inhibitory  
concns. at concns. that would be greatly exceeded in a topical preparation



L2 ANSWER 96 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1993:467857 CAPLUS

DN 119:67857

TI Antimicrobial activity and spectrum of rifaximin, a new topical rifamycin derivative

AU Hoover, William W.; Gerlach, E. Hugh; Hoban, Daryl J.; Eliopoulos, George M.; Pfaller, Michael A.; Jones, Ronald N.

CS Coll. Med., Univ. Iowa, Iowa City, IA, USA

SO Diagnostic Microbiology and Infectious Disease (1993), 16(2), 111-18

CODEN: DMIDDZ; ISSN: 0732-8893

DT Journal

LA English

AB Rifaximin, a rifamycin derivative, was evaluated in vitro to assess its spectrum and potency against a wide variety of bacteria, yeasts, viruses, and parasites. High concns. of rifaximin were often used to reflect topically achieved levels since this compound is poorly absorbed by oral route. Like rifampin, rifaximin possessed best activity against *Staphylococcus* spp. (MIC<sub>50</sub> ≤ 0.015 µg/mL), *Streptococcus* spp. (MIC<sub>50</sub>s, ≤ 0.03-0.12 µg/mL), *Enterococcus* spp. (MIC<sub>50</sub>s, 0.25-2 µg/mL), *Bacillus cereus* (MIC<sub>50</sub>, 0.06 µg/mL), *Moraxella catarrhalis* (MIC<sub>50</sub>, ≤ 0.03 µg/mL), and *Haemophilus influenzae* (MIC<sub>50</sub>, 0.25 µg/mL). Rifaximin demonstrated potential use as a topical agent for bacterial vaginosis by inhibiting *Bacteroides bivius-disiens*, *Gardnerella vaginalis*, *Lactobacillus* spp., and *Mobiluncus* spp. strains (all MICs ≤ 1 µg/mL). Strains of *Haemophilus ducreyi* and *Neisseria gonorrhoeae* (MIC<sub>50</sub>s, 0.25 µg/mL) were also inhibited. However, some organisms associated with genital tract infections were rifaximin resistant, for example, *Candida* spp., herpes virus, mycoplasmas, *Trichomonas vaginalis*, and *Ureaplasma urealyticum*. Clin. trials appear warranted using rifaximin topical concns. that will minimize mutations to rifamycin resistance.

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L2 ANSWER 97 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1993:182771 CAPLUS

DN 118:182771

TI Rifamycins as inhibitors of retroviral reverse transcriptase from M-MULV, RAV-2, and HIV-1

AU Bartolucci, Cecilia; Cellai, Luciano; Di Filippo, Patrizia; Segre, Annalaura; Brufani, Mario; Filocamo, Luigi; Brizzi, Vittorio; Benedetto, Arrigo; Di Caro, Antonino; Elia, Giuliano

CS Ist. Strutt. Chim. "G. Giacomello", Rome, Italy

SO Farmaco (1992), 47(11), 1367-83

CODEN: FRMCE8; ISSN: 0014-827X

DT Journal

LA English

AB Twenty-nine rifamycins were tested for inhibition of reverse transcriptase (RT) as potential anti HIV drugs. Two purified com. enzymes from M-MULV and RAV-2 were used. Anti-RT activity was also measured on a crude lysate of HIV-1. The results show that some derivs. have interesting levels of activity on isolated M-MULV and RAV-2 RTs, while they are less active on the RT in the crude HIV-1 lysate. The active derivs. include oximes and hydrazones, alkylaminoderivatives, open ansa-chain derivs. and derivs. carrying a modified nucleoside.

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L2 ANSWER 98 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:557735 CAPLUS

DN 117:157735

TI Application of derivative resolution of UV spectra to the quality control of rifaximine and its possible impurities

AU Corti, P.; Savini, L.; Celesti, L.; Ceramelli, G.; Montecchi, L.

CS Dip. Farm. Chim. Tecnol., Univ. Siena, Italy

SO Pharmaceutica Acta Helvetiae (1992), 67(3), 76-9

CODEN: PAHEAA; ISSN: 0031-6865

DT Journal

LA English

AB An UV spectrophotometric method with derivative resolution was developed for the

anal. of rifaximine (a synthetic rifamycin) in the presence of potential impurities of synthesis and oxidation. The method was particularly suitable for the qual. identification of the set of compds. and had good detection limits.

L2 ANSWER 99 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:433790 CAPLUS

DN 117:33790

TI Application of near-infrared reflectance spectroscopy (NIRS) to several antibiotic compounds

AU Corti, P.; Savini, L.; Dreassi, E.; Petriconi, S.; Genga, R.; Montecchi, L.; Lonardi, S.

CS Dip. Farm. Chim. Tecnol., Univ. Siena, Siena, 53100, Italy

SO Process Control and Quality (1992), 2(2), 131-42

CODEN: PCQUEJ; ISSN: 0924-3089

DT Journal

LA English

AB The possibility of applying near-IR reflectance spectroscopy (NIRS) to the qual. and quant. control of several antibiotics was investigated. Samples of amorphous sodium ampicillin, gentamycin sulfate, erythromycin ethylsuccinate, erythromycin stearate, amorphous miokamycin and rifaximin were analyzed. Some were analyzed as primary material, others half-processed (erythromycin ethylsuccinate in granules at different concns. of active ingredient) and others as the finished pharmaceutical product (rifaximin cream). The results were both qual. and quant. satisfactory. The distinction between amorphous or crystalline sodium ampicillin and ampicillin trihydrate and between the different erythromycin ethyl succinate granules was interesting. It was confirmed that NIRS can be successfully applied to the quant. control of solid and fluid (e.g. rifaximin cream) antibiotics forms.

10/728,090

L2 ANSWER 100 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:91549 CAPLUS

DN 116:91549

TI Thin-layer chromatography in the quantitative analysis of drugs.  
Determination of rifaximin and its oxidation products

AU Corti, P.; Corbini, G.; Dreassi, E.; Politi, N.; Montecchi, L.

CS Dip. Farm. Chim. Tecnol., Univ. Siena, Siena, Italy

SO Analusis (1991), 19(8), 257-61

CODEN: ANLSCY; ISSN: 0365-4877

DT Journal

LA English

AB Silica 60 HPTLC concentration zone plates were successfully used for the qual.  
and quant. determination of a semi-synthetic form of rifamycin, rifaximin,  
alone

and with its oxidation products in cream. The method also gave satisfactory  
detection limits (0.52 µg/mL) for antibiotic residues in milk after the  
cream has been used to treat mastitis in cows.

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L2 ANSWER 101 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1990:210507 CAPLUS

DN 112:210507

TI Bile rifaximin concentration after oral administration in patients undergoing cholecystectomy

AU Verardi, Stefano; Verardi, Vito

CS Clin. Chir. II, Univ. Rome, Rome, Italy

SO Farmaco (1990), 45(1), 131-5

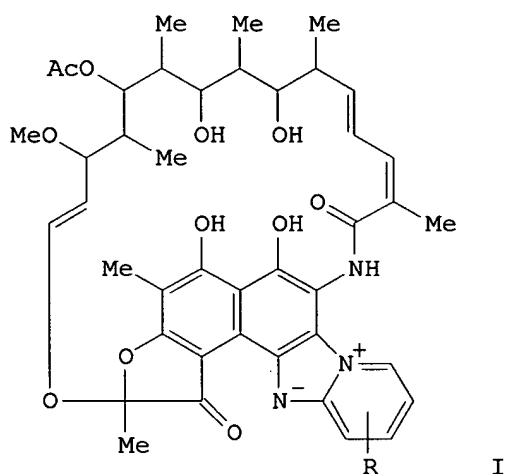
CODEN: FRMCE8; ISSN: 0014-827X

DT Journal

LA English

AB Rifaximin, a new antibiotic derived from rifamycin SV, was measured in the cholecystic bile of 13 patients submitted to cholecystectomy, after oral administration of 1600 mg of the drug in the 48 h preceding surgery. Rifaximin concns. were quantified only in 6 patients and were at least 5 times lower than those detected with rifampicin, under similar exptl. conditions. Results seem to indicate that rifaximin is virtually not adsorbed through the intestinal mucosa after oral administration.

L2 ANSWER 102 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1990:171722 CAPLUS  
DN 112:171722  
TI Structure-activity relationships in 4-deoxypyrido[1',2'-1,2]imidazo[5,4-c]rifamycin SV derivatives  
AU Cellai, L.; Cerrini, S.; Segre, A. L.; Battistoni, C.; Cossu, G.;  
Mattogno, G.; Brufani, M.; Marchi, E.; Venturini, A. P.  
CS Ist. Strutt. Chim. "Giordano Giacomello", Consiglio Naz. Ric., Rome, Italy  
SO Farmaco (1989), 44(2), 97-107  
CODEN: FRMCE8; ISSN: 0014-827X  
DT Journal  
LA English  
GI



AB Four new title compds. (I; R = 3'-Br, 3'-Cl, 3',5'-Br<sub>2</sub>, or 3',5'-Cl<sub>2</sub>) were prepared by reacting 1 equivalent of 3-bromorifamycin S with 2 equivs. of 5-bromo-, 5-chloro-, 3,5-dibromo-, or 3,5-dichloro-2-aminopyridine, resp. In mice, the new I had a better oral absorption than previously tested I (R = 5'-Me, 4'-Me, 3'-Me or H); they also had higher antibacterial activity in vivo and in vitro. XPS, NMR, and HPLC studies suggested that this was because of a higher hydrophilicity of the new compds., due to the electron-withdrawing inductive effect of the halogen atoms on the pyridoimidazo system. This effect is particularly marked at the neg. charged N-2' atom and is opposite to that of the Me group in the previously synthesized I.

L2 ANSWER 103 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1990:91306 CAPLUS

DN 112:91306

TI Toxicological profile of the new semisynthetic antibiotic Rifaximin

AU Bertoli, D.; Borelli, G.

CS Lab. Ric., Alfa Wassermann S.p.A., Italy

SO Rivista di Tossicologia: Sperimentale e Clinica (1988), 18(1), 23-39

CODEN: RTSCDD; ISSN: 0390-6019

DT Journal

LA Italian

AB The toxic effects of rifaximin, a new semisynthetic rifamycin antibiotic developed as a topical intestinal disinfectant, were studied in rats, rabbits, and dogs. The mutagenicity studies were conducted in vitro and in vivo. The oral LD50 value was > 2000 mg/kg in rats and > 3000 mg/kg in dogs. In subacute and chronic toxicity studies in rats and dogs, oral rifaximin was very well tolerated up to 100 mg/kg. The dose-dependent increase of total cholesterol observed in female rats was probably due to the effect of rifaximin on the intestinal microbial flora. Oral rifaximin, up to 100 mg/kg, had no teratogenic effects in rats and rabbits and did not influence the development of the rat pups. Rifaximin showed good fertility rates and no changes in the gestation length and survival of offspring to the highest dose of 100 mg/kg. The drug had no mutagenic effects.



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L2 ANSWER 104 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1988:75114 CAPLUS

DN 108:75114

TI New process for the synthesis of imidazo rifamycins

IN Cannata, Vincenzo; Tamagnone, Gain F.; Piani, Silvano; Campana, Manuela;  
Da Roit, Giovanni

PA Alfa Farmaceutici S.p.A., Italy

SO Can., 30 pp.

CODEN: CAXXA4

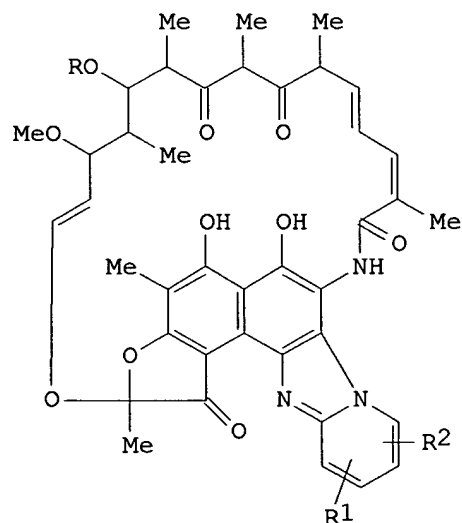
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 1215976	A1	19861230	CA 1985-480320	19850429
	DK 8502145	A	19851116	DK 1985-2145	19850514
	DK 160829	B	19910422		
	DK 160829	C	19911007		
	FI 8501908	A	19851116	FI 1985-1908	19850514
	FI 83874	B	19910531		
	FI 83874	C	19910910		
	NO 8501920	A	19851118	NO 1985-1920	19850514
	NO 164030	B	19900514		
	NO 164030	C	19900822		
	ES 543116	A1	19860101	ES 1985-543116	19850514
	AT 8501450	A	19880315	AT 1985-1450	19850514
	AT 386829	B	19881025		
PRAI	IT 1984-3464	A	19840515		
	IT 1984-3465	A	19840515		

GI



I

AB Imidazorifamycins I [R = H, Ac; R1, R2 = H, alkyl, PhCH2O, (di)alkylaminoalkyl, alkoxyalkyl, hydroxyalkyl, cyano, halo, NO2, SH, alkyl-, phenylthio, CONH2, (di)alkylcarbamoyl; R1R2 complete a benzene ring (un)substituted by 1 or 2 Me or Et] were prepared Rifamycin S (0.007 mol), 0.021 mol 2-amino-4-methylpyridine, and 0.0035 mol iodine in CH2Cl2 were stirred at room temperature 30 h and the mixture was treated with 20%

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ascorbic acid to give 76% 4-deoxy-4'-methylpyrido[1',2':1,2]imidazo[5,4-c]rifamycin SV. I have outstanding antibacterial properties in vitro and in vivo and are very useful in combating gastrointestinal microbial infections.

10/728,090

L2 ANSWER 105 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1988:34706 CAPLUS

DN 108:34706

TI In vitro antibacterial activity of rifaximin against *Clostridium difficile*, *Campylobacter jejunii* and *Yersinia* spp

AU Ripa, S.; Mignini, F.; Prenna, M.; Falcioni, E.

CS Dep. Cell. Biol., Univ. Camerino, Camerino, 62032, Italy

SO Drugs under Experimental and Clinical Research (1987), 13(8), 483-8

CODEN: DECRDP; ISSN: 0378-6501

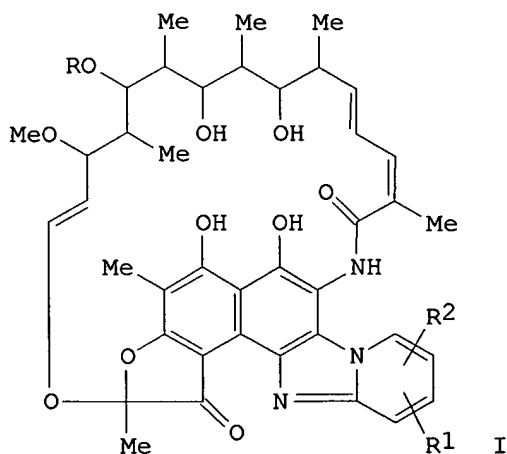
DT Journal

LA English

AB Fifty-four isolates of *C. jejunii*, 91 isolates of *Yersinia* and 56 isolates of *C. difficile*, recovered from stools of patients with diarrhea or other intestinal disturbances and from stools of asymptomatic patients receiving antibiotic therapy, were tested in vitro for susceptibility to rifaximin, rifampicin and neomycin. The in vitro antibacterial activities were comparable against the aerobic bacterium; on the contrary, against microaerophilic and anaerobic bacteria rifaximin and rifampicin were much more effective than neomycin.

L2 ANSWER 106 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1987:617369 CAPLUS  
DN 107:217369  
TI Process for the synthesis of pyridoimidazorifamycins as antibacterials  
IN Cannata, Vincenzo; Tamagnone, Gian F.; Campana, Manuela; Piani, Silvano;  
Alpino, Raul R.  
PA Alfa Farmaceutici S.p.A., Italy  
SO Can., 22 pp.  
CODEN: CAXXA4  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 1218650	A1	19870303	CA 1985-491511	19850925
	ES 547265	A1	19860216	ES 1985-547265	19850925
	DK 8504349	A	19860327	DK 1985-4349	19850925
	DK 161706	B	19910805		
	DK 161706	C	19920120		
	FI 8503683	A	19860327	FI 1985-3683	19850925
	FI 83875	B	19910531		
	FI 83875	C	19910910		
	NO 8503771	A	19860401	NO 1985-3771	19850925
	NO 165107	B	19900917		
	NO 165107	C	19901227		
	AT 8502797	A	19880415	AT 1985-2797	19850925
	AT 387020	B	19881125		
PRAI	IT 1984-3581	A	19840926		
GI					



AB Title compds. I (R = H, Ac; R1,R2 = H, C1-4 alkyl, PhCH2O, mono-, di-C1-3 alkylamino-C1-4-alkyl, cyano, halo, O2N, HS, etc.; R1R2 with 2 consecutive C's of the pyridine nucleus, form (un)substituted benzene ring), useful as antibacterials (no data), were prepared A mixture of rifamycin B, 2-amino-4-methylpyridine, and iodine in CH2Cl2 was kept at room temperature for 15 h to give 4-deoxy-4'-methylpyrido[1',2':1,2]imidazo[5,4-c]rifamycin SV.

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L2 ANSWER 107 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1987:583579 CAPLUS

DN 107:183579

TI Veterinary composition containing antimicrobial agents for treatment of mastitis by intramammary administration

IN Montecchi, Lauretta; Verardi, Paolo

PA Fatro S.p.A., Italy

SO Eur. Pat. Appl., 7 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	EP 222712	A2	19870520	EP 1986-830320	19861104
	EP 222712	A3	19871119		
	EP 222712	B1	19900606		
	R: AT, BE, CH, DE, ES, FR, GB, GR, LI, NL, SE				
	AT 53300	E	19900615	AT 1986-830320	19861104
PRAI	IT 1985-3595	A	19851108		
	EP 1986-830320	A	19861104		

AB A veterinary composition for the prevention and cure of mastitis, especially bovine

mastitis, and intended for intramammary injection comprises at least 1 antimicrobial agent dispersed in a mixture containing triglycerides of palmitic and stearic acid and polyoxyethenylated cetyl and stearyl alcs., and held in an oily medium of mineral, vegetable, synthetic or mixed extraction A composition contained Na cephalixin 6, triglycerides of palmitic and stearic acid 10, polyoxyethenylated cetyl and stearyl alc. 2.5, and peanut oil 81.5 g.

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L2 ANSWER 108 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1987:508809 CAPLUS

DN 107:108809

TI Transcutaneous absorption of a topical rifamycin preparation: rifaximin  
(L/105)

AU Venturini, A. P.; Bertoli, D.; Marchi, E.

CS Alfa Ric. S.p.A., Bologna, Italy

SO Drugs under Experimental and Clinical Research (1987), 13(4), 231-2

CODEN: DECRDP; ISSN: 0378-6501

DT Journal

LA English

AB The transcutaneous absorption of a new rifamycin preparation, rifaximin, was compared with that of rifampicin in the rat. Contrary to what was observed for rifampicin, only traces of or no rifaximin absorbed.

L2 ANSWER 109 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1987:60751 CAPLUS

DN 106:60751

TI Renal excretion of L-105, a new cephalosporin antibiotic in dogs

AU Matsumoto, Fumio; Inokawa, Yoshiyuki; Akai, Nobuko; Takei, Hiroshi; Hiruma, Hideo

CS Dep. Intern. Med., Kanagawa Prefect. Midwives Nurses Training Sch. Hosp., Kanagawa, Japan

SO Chemotherapy (Tokyo) (1986), 34(Suppl. 3), 100-4

CODEN: NKRZAZ; ISSN: 0369-4682

DT Journal

LA Japanese

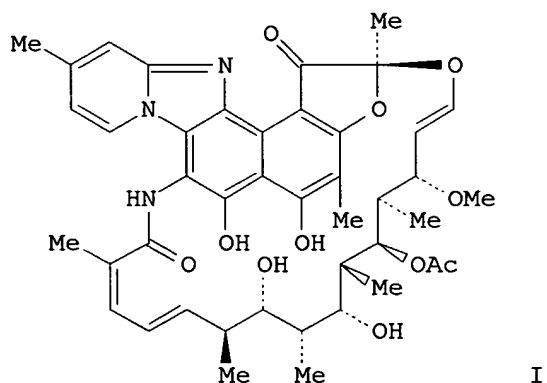
AB The mechanism of renal excretion of L-105 [80621-81-4] was investigated in dogs with cannula inserted into the ureter. The pelvic urine was collected in fractions and the phase of distal tubular excretion, proximal tubular excretion and glomerular filtration were ascertained by monitoring concns. of Na<sup>+</sup>/K<sup>+</sup> ions, p-aminohippuric acid, and inulin in each fraction. The concentration of creatinine was monitored as

a parameter of urine concentration No specific peak of L-105 was recognized in the

phase of p-aminohippuric acid excretion nor in the entire phase of Na<sup>+</sup>/K<sup>+</sup> reabsorption in dogs. After pretreatment with probenecid (30 mg/kg), the peak of p-aminohippuric acid disappeared while the stop-flow pattern of L-105 remained virtually unchanged. Thus, the renal excretion of L-105 took place mainly through glomerular filtration in dogs.

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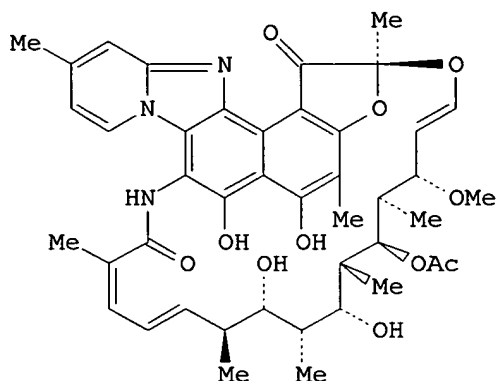
L2 ANSWER 110 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1986:583465 CAPLUS  
DN 105:183465  
TI Acute, subacute, chronic toxicity and mutagenicity studies of rifaximin  
(L/105) in rats  
AU Borelli, G.; Bertoli, D.  
CS Alfa Ric. S.p.A., Bologna, 40133, Italy  
SO Chemioterapia (1986), 5(4), 263-7  
CODEN: CHEMEV; ISSN: 0392-906X  
DT Journal  
LA English  
GI



AB Acute, subacute, and chronic toxicity-mutagenicity studies of rifaximin (L/105) (I) [80621-81-4], a new semisynthetic rifamycin SV antibiotic, were conducted in rats. The oral LD50 value for this species was >2000 mg/kg. Rifaximin given orally to rats up to 6 mo produced no evident adverse effects up to 100 mg/kg. The moderate effects noted were probably due to the topical action of the drug. Rifaximin did not show any mutagenic activity when compared with mutagenic stds.



L2 ANSWER 111 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1986:583464 CAPLUS  
DN 105:183464  
TI In vitro and in vivo evaluation of L/105, a new topical intestinal rifamycin  
AU Venturini, A. P.; Marchi, E.  
CS Alfa Ric. S.p.A., Bologna, 40133, Italy  
SO Chemioterapia (1986), 5(4), 257-62  
CODEN: CHEMEV; ISSN: 0392-906X  
DT Journal  
LA English  
GI



AB L/105 (rifaximin) (I) [80621-81-4] is a new rifamycin active in vitro against both gram-pos. and gram-neg. microorganisms. The activity of L/105 was comparable to that of rifampicin and, against gram-pos. bacteria, higher than that of neomycin. The antibacterial activities of L/105 and rifampicin were equally affected by the highest size of inoculum used (10 cells/mL) and they were equally bactericidal against *Staphylococcus aureus* and *Escherichia coli*. The speed and the degree of development of resistance to L/105 were quite superimposable on those of neomycin. In vivo, L/105 did not show therapeutic activity by oral route in the staphylococcal infection in the mouse till the highest dosage used (10 mg/kg); under the same conditions, gentamicin was equally ineffective. After s.c. administration, L/105 showed therapeutic activity (ED<sub>50</sub> = 0.46 mg/kg) practically superimposable on that of orally administered rifampicin.

10/728,090

L2 ANSWER 112 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1986:545708 CAPLUS

DN 105:145708

TI Fertility study of rifaximin (L/105) in rats

AU Bertoli, D.; Borelli, G.

CS Alfa Ric. S.p.A., Bologna, 40133, Italy

SO Chemioterapia (1986), 5(3), 204-7

CODEN: CHEMEV; ISSN: 0392-906X

DT Journal

LA English

AB The effects of rifaximin [80621-81-4] on conception and pregnancy in rats up to F1 progeny are reported. Rifaximin had no effect on fertility rate. No differences in the number of viable or dead fetuses per litter (F0 progeny) were seen between untreated controls and those treated with I up to 100 mg/kg. The number of live or dead pups at birth, pup weight, gestation length and survival of offspring to weaning were not influenced up to the highest dose, 100 mg/kg (F0-F1 progeny).

10/728,090

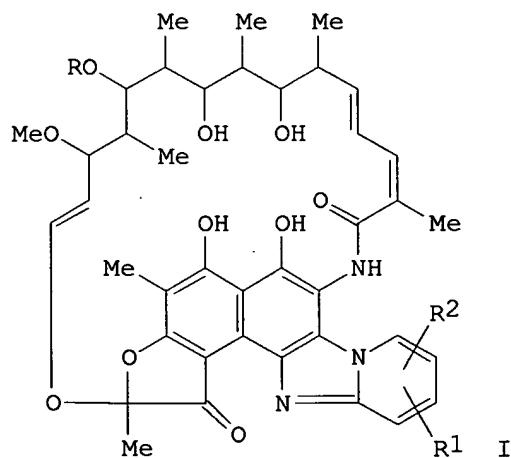
L2 ANSWER 113 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1986:207057 CAPLUS  
DN 104:207057  
TI Pyridoimidazorifamycins  
IN Cannata, Vincenzo; Tamagnone, Gian Franco; Piani, Silvano  
PA Alfa Farmaceutici S.p.A., Italy  
SO Eur. Pat. Appl., 26 pp.  
CODEN: EPXXDW

DT Patent  
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 161534	A2	19851121	EP 1985-104790	19850419
	EP 161534	A3	19870304		
	EP 161534	B1	19890920		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	ZA 8502971	A	19851224	ZA 1985-2971	19850419
	AT 46512	E	19891015	AT 1985-104790	19850419
	US 4557866	A	19851210	US 1985-727521	19850426
	CA 1215708	A1	19861223	CA 1985-480321	19850429
	DK 8502146	A	19851116	DK 1985-2146	19850514
	DK 162647	B	19911125		
	DK 162647	C	19920413		
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	FI 81101	B	19900531		
	FI 81101	C	19900910		
	NO 8501921	A	19851118	NO 1985-1921	19850514
	NO 164242	B	19900605		
	NO 164242	C	19900912		
	JP 60252483	A2	19851213	JP 1985-102528	19850514
	JP 04069634	B4	19921106		
	ES 543115	A1	19860101	ES 1985-543115	19850514
	AU 8542515	A1	19851121	AU 1985-42515	19850515
	AU 568934	B2	19880114		
PRAI	IT 1984-3463	A	19840515		
	EP 1985-104790	A	19850419		

GI



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AB The title compds. I [R = H, Ac; R1, R2 = H, C1-4 alkyl, PhCH2O, cyano, halo, NO2, SH, etc.; R1R2 and 2C of the pyridine form a (un)substituted benzene ring], useful as in vitro and in vivo antibacterials (no data), were prepared by the reaction of rifamycin O (II) with a substituted 2-aminopyridine. Thus, II was reacted with 2-amino-4-methylpyridine in CH2Cl2 to give 4-deoxy-4'-methylpyrido[1',2:1,2]imidazo[5,4-c]rifamycin SV.

# I

AB Tritiated rifaximin (I) [80621-81-4] was administered in a single oral dose of 10 mg/kg or 100 mg/kg to rats. After treatment, at fixed times, the animals were sacrificed and the radioactivity in plasma, urine, feces, and in the principal organs and tissues was measured. The radioactivity present in the feces of the two groups of rats was > 95% of the administered dose, while the amts. found in the urine ranged between 1.15% and 1.5% of the dose. In the plasma and tissues the radioactivity levels were very low. Thus, I is not absorbed from the intestine to any significant amount

L2 ANSWER 115 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1985:464370 CAPLUS

DN 103:64370

TI A study of structure-activity relationships in 4-deoxypyrido[1',2'-1,2]imidazo[5,4-c]rifamycin SV derivatives by electron spectroscopy for chemical analysis and proton NMR

AU Cellai, Luciano; Cerrini, Silvio; Segre, Annalaura; Battistoni, Claudio; Cossu, Gianni; Mattogno, Giulia; Brufani, Mario; Marchi, Egidio

CS Istit. Strutt. Chim. "Giordano Giacomello", Cons. Naz. Ric., Rome, Italy

SO Molecular Pharmacology (1985), 27(1), 103-8

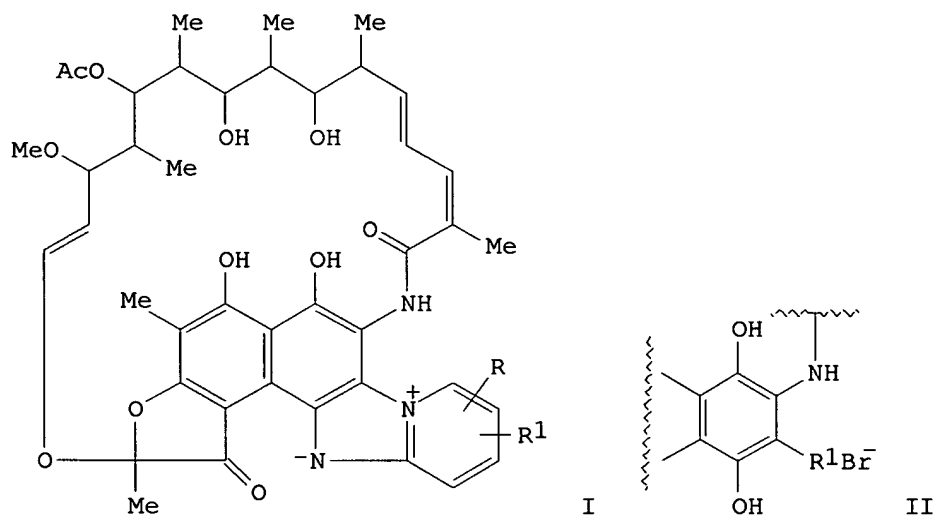
CODEN: MOPMA3; ISSN: 0026-895X

DT Journal

LA English

AB A new class of rifamycins, 4-deoxypyrido[1',2'-1,2]imidazo[5,4-c]rifamycin SV derivs. are potent antibacterial agents and are not absorbed at the gastrointestinal level and can therefore probably be used as antibacterial intestinal disinfectants. From the present x-ray, electron spectroscopy for chemical anal., and <sup>1</sup>H NMR study, it appears that this peculiar pharmacokinetic behavior is mainly attributed to the fact that the pyridoimidazo system exists in these compds. in a mesomeric betaine form, bearing one pos. and one neg. charged nitrogen. If it is assumed that rifamycins are generally absorbed by passive diffusion, the presence of the 2 oppositely charged nitrogens, together with the presence of the phenolic hydroxyls, means that these mols. are ionized at all pH values encountered along the gastrointestinal tract, which thus prevents their absorption. These mols. also display a strong tendency to self-associate both in solution and in the solid state, and the increase in mol. size may also play a role in preventing their absorption.

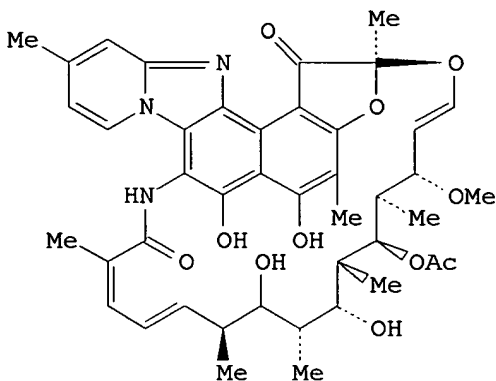
L2 ANSWER 116 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1985:437255 CAPLUS  
 DN 103:37255  
 TI 4-Deoxyprido[1',2':1,2]imidazo[5,4-c]rifamycin SV derivatives. A new series of semisynthetic rifamycins with high antibacterial activity and low gastroenteric absorption  
 AU Marchi, Egidio; Mascellani, Giuseppe; Montecchi, Laura; Venturini, Anna Paolo; Brufani, Mario; Cellai, Luciano  
 CS Alfa Farm. S.p.A., Bologna, 40133, Italy  
 SO Journal of Medicinal Chemistry (1985), 28(7), 960-3  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DT Journal  
 LA English  
 OS CASREACT 103:37255  
 GI



AB Title compds. I (R = 3-Me, 4-Me, 5-Me, 3-OCH<sub>2</sub>Ph, H, R<sub>1</sub> = H; RR<sub>1</sub> = 4,5-CH:CHCH:CH) were prepared that demonstrated high antibacterial activity suitable for an intestinal disinfectant. I are zwitterionic and are poorly absorbed through the gastroenteric tract but maintain the ability to cross the bacterial cell wall. The structure-activity relationship of I is discussed and the derivative with the highest ratio between s.c. and oral activity (I, R = 4-Me, R<sub>1</sub> = H) was selected for clin. development. Several 3-(quaternary ammonium bromides) II (R<sup>+</sup> = N<sup>+</sup>Et<sub>3</sub>, pyridinio, 3-methoxycarbonylpyridinio, 3-carbamoylpyridinio) were prepared and tested for antibacterial activity. II were too polar to even cross the bacterial cell wall.

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L2 ANSWER 117 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1985:403518 CAPLUS  
DN 103:3518  
TI In vitro activity of rifaximin and rifampicin against some anaerobic  
bacteria  
AU Lamanna, A.; Orsi, A.  
CS Lab. Batteriol. Virol., USL, Florence, 50134, Italy  
SO Chemioterapia (1984), 3(6), 365-7  
CODEN: CHEMEV; ISSN: 0392-906X  
DT Journal  
LA English  
GI

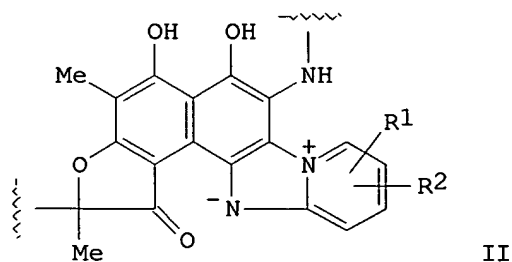
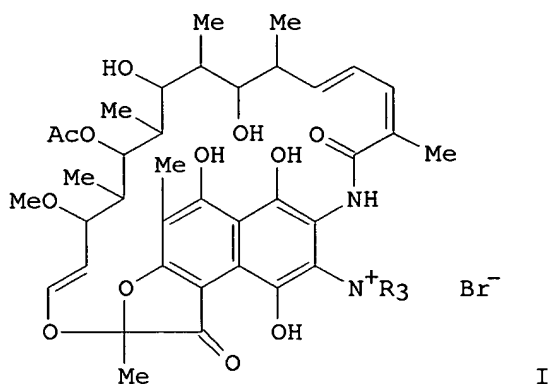


I

AB Activity of rifampicin and of a new rifamycin, rifaximin (I) was tested in strains of anaerobic bacteria belonging to the *Bacteroides* genus (75 *B. fragilis* group and 17 *Bacteroides non-fragilis* group) and in *Clostridium perfringens* (15 strains). The bactericidal activity of both rifamycins overlapped and equaled 100% in the case of the non-fragilis *Bacteroides* and *Clostridium* species.



L2 ANSWER 118 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1985:184882 CAPLUS  
 DN 102:184882  
 TI The synthesis of 4-deoxypyrido[1',2'-1,2]imidazo[5,4-c]rifamycin SV derivatives  
 AU Brufani, Mario; Cellai, Luciano; Marchi, Egidio; Segre, Annalaura  
 CS Gruppo Chim. Biol. Strutt. Chim., Univ. "La Sapienza", Rome, 00185, Italy  
 SO Journal of Antibiotics (1984), 37(12), 1611-22  
 CODEN: JANTAJ; ISSN: 0021-8820  
 DT Journal  
 LA English  
 GI

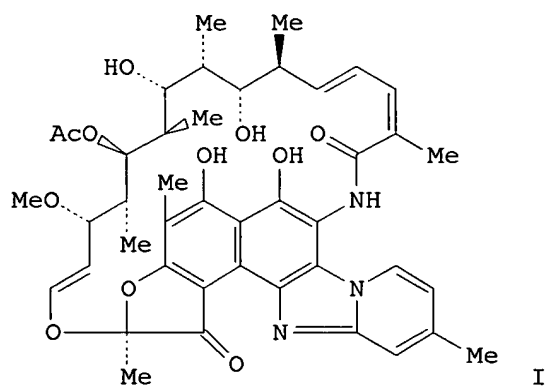


AB Two series of new semisynthetic rifamycin SV derivs. I [ $N+R_3 = N+Et_3$ , (un)substituted pyridinium] and II ( $R_1 = H, 3-Me, 4-Me, 5-Me, 3-OCH_2Ph$ ,  $R_2 = H$ ;  $R_1R_2 = 3,4-CH:CH:CH$ ) have been prepared. The intermediate rifamycins S were also isolated. Whereas I had poor antibacterial activity in vitro, II were highly active in vitro but poorly absorbed in vivo. They could thus have potential as agents in the therapy of intestinal infections.

10/728,090

L2 ANSWER 119 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1984:570913 CAPLUS  
DN 101:170913  
TI L/105 a new semisynthetic derivative of rifamycin SV, synthesis and  
structure-activity relationship  
AU Marchi, E.; Mascellani, G.; Montecchi, L.; Brufani, M.; Cellai, L.  
CS Alfa Farm. S.p.A., Bologna, Italy  
SO Chemioterapia (1983), 2(5, Suppl.: Mediterr. Congr. Chemother., Proc.,  
3rd, 1982), 48-50  
CODEN: CHEMEV; ISSN: 0392-906X  
DT Journal; General Review  
LA English  
AB A review with 2 refs.

L2 ANSWER 120 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1984:503607 CAPLUS  
 DN 101:103607  
 TI Structure-activity relationships in 4-deoxypyrido(1',2'-1,2)imidazo(5,4-c)rifamycin SV derivatives  
 AU Cellai, L.; Cerrini, S.; Brufani, M.; Marchi, E.; Mascellani, G.; Montecchi, L.  
 CS Ist. Strutt. Chim. "G. Giacomello", Rome, Italy  
 SO Chemioterapia (1983), 2(5, Suppl.: Mediterr. Congr. Chemother., Proc., 3rd, 1982), 53-4  
 CODEN: CHEMEV; ISSN: 0392-906X  
 DT Journal  
 LA English  
 GI



AB The polarity of rifamycin L-105 SV (I) [80621-81-4] and its oxidized S [80621-76-7] form and the contribution of this polarity in the pharmacokinetics of these drugs were investigated. NMR and x-ray crystallog. studies indicated that the pyridoimidazo ring is coplanar with the naphthoquinonic nucleus making the pyridoimidazo ring system aromatic with the 2 N both charged. The pyrido-N is pos. charged and the other neg. charged. The contribution of charged forms to the resonance-structure of these compds. renders these agents with pharmacokinetic properties that make them virtually nonabsorbable from the intestine and thus providing high antimicrobial activity in the digestive tract.

10/728,090

L2 ANSWER 121 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1984:465616 CAPLUS  
DN 101:65616  
TI Teratogenic effect of rifaximin on rats and rabbits and its influence on  
rat perinatal development  
AU Bertoli, D.; Borelli, G.  
CS Lab. Tossicol., Alfa Ric. S.p.A., Bologna, Italy  
SO Bollettino - Societa Italiana di Biologia Sperimentale (1984), 60(5),  
1079-85  
CODEN: BSIBAC; ISSN: 0037-8771  
DT Journal  
LA Italian  
AB Rifaximin [88747-56-2], given orally at 50 or 100 mg/kg/day to  
rats and rabbits during the organogenesis period of pregnancy, was devoid  
of teratogenic activity. The drug also did not affect the phys. or  
behavioral development of rat pups when it was given to the mothers during  
the last drug of pregnancy and during lactation.

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L2 ANSWER 122 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1984:400201 CAPLUS  
DN 101:201  
TI L/105: report on pharmacokinetics in rats, dogs, after oral  
administration and adverse reactions  
AU Venturini, A. P.  
CS Res. Lab., Alfa Farm. S.p.A., Bologna, Italy  
SO Chemioterapia (1983), 2(5, Suppl.: Mediterr. Congr. Chemother., Proc.,  
3rd, 1982), 162-3  
CODEN: CHEMEV; ISSN: 0392-906X  
DT Journal  
LA English  
AB In dogs and rats given oral doses of the new rifamycin L/105 [ **80621-81-4**], very little of the drug was absorbed by the gastrointestinal tract, most being eliminated in the feces. The antibiotic was well tolerated even after chronic administration and appears to be a suitable intestinal antibiotic.

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L2 ANSWER 123 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1984:61494 CAPLUS  
DN 100:61494  
TI Indomethacin-induced intestinal lesions and fecal flora  
AU Benoni, G.; Cuzzolin, L.; Raimondi, M. G.; Velo, G. P.  
CS Inst. Pharmacol., Univ. Verona, Verona, 37134, Italy  
SO Advances in Inflammation Research (1984), 6, 103-8  
CODEN: ADIRDF; ISSN: 0197-8322  
DT Journal  
LA English  
AB In rats, administration of some antibiotics such as neomycin [1404-04-2] caused a decrease in ulcers induced by indomethacin [53-86-1], accompanied by a decrease of aerobic and anaerobic bacterial fecal flora, suggesting that protection against indomethacin-induced lesions can be ascribed to an inhibition of intestinal bacterial flora growth. The specific microorganisms involved in the development of indomethacin-induced lesions appear to be bacteroides, coliforms, and gram-pos. bacteria.

10/728,090

L2 ANSWER 124 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1983:119073 CAPLUS  
DN 98:119073  
TI Pharmacokinetics of L/105, a new rifamycin, in rats and dogs, after oral administration  
AU Venturini, A. P.  
CS Res. Lab., Alfa Farm. S.p.A., Bologna, I-40133, Italy  
SO Chemotherapy (Basel, Switzerland) (1983), 29(1), 1-3  
CODEN: CHTHBK; ISSN: 0009-3157  
DT Journal  
LA English  
AB The absorption and tissue distribution of a new rifamycin, L/105 [80621-81-4] were studied in rats after oral administration of 100 mg/kg. L/105, contrary to what was observed for rifampicin, was not absorbed since neither serum nor tissue levels were observed. Also, in dogs after oral administration of L/105 in a single dose (25 mg/kg) and in multiple doses (10 mg/kg/day, for 8 days), no traces of the compound were detected in the serum. The elimination of L/105 was investigated in the rat. The highest recovery of L/105 (>50% of the administered dose) was in the feces after 72 h; hardly any L/105 was found in the urine.

10/728,090

L2 ANSWER 125 OF 125 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1982:68719 CAPLUS  
DN 96:68719  
TI Imidazorifamycin derivatives with antibacterial activity  
PA Alfa Farmaceutici S.p.A., Italy  
SO Belg., 40 pp.  
CODEN: BEXXAL  
DT Patent  
LA French  
FAN.CNT 1

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PI	BE 888895	A1	19810916	BE 1981-59169	19810521
	NL 8102290	A	19811216	NL 1981-2290	19810511
	NL 187022	B	19901203		
	NL 187022	C	19910501		
	US 4341785	A	19820727	US 1981-262123	19810511
	AU 8170655	A1	19811126	AU 1981-70655	19810518
	AU 537093	B2	19840607		
	AT 8102227	A	19830615	AT 1981-2227	19810519
	AT 373599	B	19840210		
	FR 2482967	A1	19811127	FR 1981-10058	19810520
	FR 2482967	B1	19850329		
	DK 8102247	A	19811123	DK 1981-2247	19810521
	DK 157876	B	19900226		
	DK 157876	C	19900730		
	FI 8101565	A	19811123	FI 1981-1565	19810521
	FI 69467	B	19851031		
	FI 69467	C	19860210		
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	NO 155622	B	19870119		
	NO 155622	C	19870429		
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	SE 453089	B	19880111		
	SE 453089	C	19880421		
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	ZA 8103430	A	19820630	ZA 1981-3430	19810521
	CA 1142518	A1	19830308	CA 1981-378015	19810521
	GB 2079270	A	19820120	GB 1981-15790	19810522
	GB 2079270	B2	19840118		
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	JP 61023192	B4	19860604		
	DE 3120460	A1	19820311	DE 1981-3120460	19810522
	DE 3120460	C2	19901213		
	CH 648037	A	19850228	CH 1981-3381	19810522
PRAI	IT 1980-3429	A	19800522		
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Treating halorifamycins with 2-aminopyridines gave pyridoimidazorifamycins I and II [R, R1 = H, alkyl, OCH2Ph, aminoalkyl, alkoxyalkyl, CH2OH, hydroxyalkyl, NO2; RR1 = (un)substituted benzo; R2 = H, Ac], which exhibited bactericidal activity. Thus, stirring 3-bromorifamycin S and 2-amino-4-methylpyridine in EtOH at room temperature gave I (R = Me, R1 = H, R2 = Ac).



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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN

RN 80621-81-4 REGISTRY

ED Entered STN: 16 Nov 1984

CN 2,7-(Epoxy-pentadeca[1,11,13]trienimino)benzofuro[4,5-e]pyrido[1,2-a]benzimidazole-1,15(2H)-dione, 25-(acetyloxy)-5,6,21,23-tetrahydroxy-27-methoxy-2,4,11,16,20,22,24,26-octamethyl-, (2S,16Z,18E,20S,21S,22R,23R,24R,25S,26R,27S,28E)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2,7-(Epoxy-pentadeca[1,11,13]trienimino)benzofuro[4,5-e]pyrido[1,2-a]benzimidazole-1,15(2H)-dione, 25-(acetyloxy)-5,6,21,23-tetrahydroxy-27-methoxy-2,4,11,16,20,22,24,26-octamethyl-, [2S-(2R\*,16Z,18E,20R\*,21R\*,22S\*,23S\*,24S\*,25R\*,26S\*,27R\*,28E)]-

OTHER NAMES:

CN L 105

CN L 105 (ansamacrolide antibiotic)

CN L 105SV

CN Rifamycin L 105

CN Rifamycin L 105SV

CN **Rifaximin**

DR 126334-60-9, 88747-56-2

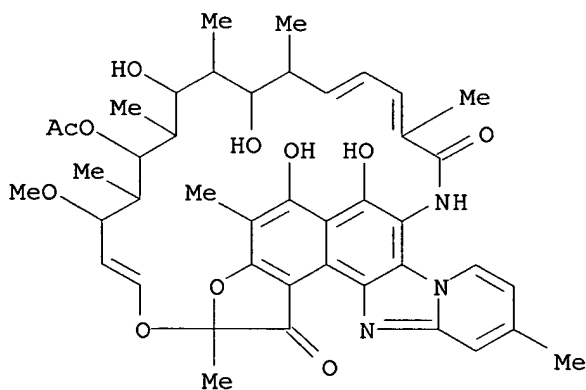
MF C43 H51 N3 O11

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, DDFU, DIOGENES, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: WHO



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

124 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

125 REFERENCES IN FILE CAPLUS (1907 TO DATE)

10/728,090

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(FILE 'REGISTRY' ENTERED AT 08:45:16 ON 16 SEP 2005)

DEL HIS

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FILE 'CAPLUS' ENTERED AT 08:45:45 ON 16 SEP 2005

L2 125 S L1

FILE 'REGISTRY' ENTERED AT 08:46:34 ON 16 SEP 2005

FILE 'CAPLUS' ENTERED AT 08:46:35 ON 16 SEP 2005

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.45

342.00

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-91.25

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